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PELLAGRA: THEORIES OF CAUSATION.

A Critical Review.

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Pellagra is a rare disease in Great Britain and seldom mentioned until recent years, when it has become the custom in dealing with so-called deficiency diseases to make some brief reference to the condition. In those countries, however, in which it has been endemic, pellagra has excited a great deal of attention and study, and it would be difficult to find any other malady in the whole realm of morbid conditions concerning which so many theories have been propounded. To enumerate them would be to recount the advances in medical thought, and one might add fashion, during two centuries, from miasm to monophagism, from vicious humours to avitaminosis and ultra-microscopic virus.

Gherardini writing on pellagra in 1780, quoted by H. F. Harris (1919)*, remarked "All things may be established theoretically. Error itself may be proved; this is an undeniable axiom, which is particularly true of medicine. The majority of physicians have ever preferred with an appearance of belief, the effulgent chimeras of their fancy to the wise teachings of nature. Piling conclusion on conclusion, they, with cunning art, explore the boundless realms of theoretical medicine, and soaring to their hearts' content, prefer the vainglory of having advanced an hypothesis to slow and painful investigation, particularly as in the primrose pathway of theory they find no difficulties which interfere with their conclusions." Other authors of more recent times have been inspired, in similar phraseology, to hurl sarcastic criticism upon those who have ventured to theorize upon the causation of pellagra.

F. M. Sandwith remarked "The field of pellagrous aetiology has been the playground of fledglings whose intellectual judgment is befuddled because they have no real comprehension of the fundamental

References marked * are given in bibliography, this *Bulletin*, 1936, Vol. 33, pp. 897–901.

question and, therefore, attempt to introduce into the aetiology of pellagra all sorts of things from bald banalities to the most wonderful fantasies."

A. D. BIGLAND (1920)* in thus quoting SANDWITH, intimated that these words should never be forgotten by those who would enter this field of discussion. They are the more pointed as some of SANDWITH's teachings have since been found to need modification. SANDWITH for example was responsible for writing (1898) " In no case can pellagra be accurately diagnosed unless the man comes from a country where maize is a staple article of diet," a dictum now recognized as untrue.

BIGLAND, after quoting SANDWITH, went on to say " for some years I have thought the only way to discover the cause of a disease like pellagra was to make, as it were, an arm-chair study of all the cases the world over. The question will then resolve itself into a review of the similarities and dissimilarities presented by the various outbreaks, with the hope that in the end the research may reveal a factor common to all." Some such idea had occurred to the present writer and as a result of a study extending over many years there have emerged a few fairly definite impressions, some of which will here be discussed, firstly the theories of causation of pellagra and secondly theories concerning the pathogenesis of some of the symptoms.

The majority of those who have written upon the subject have based their theories in regard to causation upon observations limited to some one group of cases, under certain local conditions. They have often ignored the findings of others or treated them with not always polite contempt. Cases of the disease which did not fit some particular theory were either gently left out of the picture or conveniently elevated to the rank of pseudopellagra, para-pellagra, alcoholic pellagra, secondary pellagra, etc.

On the other hand, a study of these exceptional cases, those that have not fitted into the theory of the moment, should go a long way towards suggesting the key to the whole problem.

Many of the theories of the past probably contain truths in so far as they may be regarded as factors of aetiological importance, always bearing in mind the necessity of putting oneself in the place of the author when interpreting his writings.

In venturing to put forward, from an armchair, any ideas concerning the causation of pellagra, an attempt will be made to explain some of the known facts concerning that disease and at the same time to correlate the theories of others, no one of which has ever received general acceptance.

The many theories will not be set out in a list but merely alluded to as occasion arises. Many will require but a short reference, others will need more attention, including two as representative of medical opinion of to-day—the one which suggests that pellagra is due to a deficiency of " protein of high biological value " in the diet, the second which suggests that it is an avitaminosis.

During the years which have elapsed since CASTLE and his colleagues enunciated their theory to explain the pathogeny of pernicious anaemia, a similar pathogeny has been suggested for a number of other conditions including first, sub-acute combined degeneration of the cord, then some other forms of anaemia and lastly what has been called by A. H. DOUTHWAITE (1936) gastrogenous polyneuritis. It seems possible that the underlying principle will be found to have a still wider application.

A number of observers have, of course, remarked some of the resemblances between pellagra and pernicious anaemia. That some faulty reaction, such as is believed to occur in pernicious anaemia and these other conditions, may take place in pellagra must have crossed the minds of many of them.

In the discussion which follows it is proposed to examine the problem of pellagra in the light of such an hypothesis, an exercise which, as far as I am aware, has never been undertaken.

That the "*fons et origo mali* (*pellagrae*)" is located in the stomach is suggested by the many analogies with pernicious anaemia, etc.

In these several conditions and pellagra we see linked together in various combinations disturbances in function of the haemopoietic system and the nervous system associated with chronic gastritis and failure of the normal secretion of hydrochloric acid by the stomach as if the hand of chronic gastritis struck different chords on the keyboard of gastric secretion.

But whereas in pernicious anaemia the fault is considered to lie in a defective secretion of the intrinsic factor by the " pyloric gland organ " as E. MEULENGRACHT (1935) calls it, in pellagra it is here suggested there may be default of one or other or both intrinsic and extrinsic factors (to be referred to as P.I.F. and P.E.F.).

In endemic pellagra both factors are probably involved, in sporadic pellagra a failure of P.I.F. may play the more important part.

At the present time both the current theories postulate a deficiency state ; in the one, so stoutly defended by W. H. WILSON (1918, 1921,* 1930) a deficiency of protein of " high biological value," in the other an avitaminosis. In the latter the lack of vitamin alone is presumed to cause the disease, or the symptoms of the malady are supposed to be caused by an hypothetical toxamin, as suggested by E. MELLANBY (1934), derived from grain, which in the absence of the vitamin is not neutralized. Neither of these theories would appear to cover all the ground as has been shown by the arguments advanced by their respective adherents against their opponents.

While it is admitted that endemic pellagra is associated with an ill-balanced monotonous diet consisting principally of grain, with a minimum of those substances which contain so-called protein of high biological value, and a full vitamin content, the fact that large native populations in Africa and elsewhere subsist on similar diets without developing pellagra is generally lost sight of and left unexplained.

When J. GOLDBERGER* put forward his thesis of a food deficiency and postulated his P.P. factor in the prevention of pellagra, he was, it is suggested, only half-way towards reaching the truth. This P.P. factor was later referred to in America as Vitamin G, and by some identified with Vitamin B_2.

Since then, however, what is now referred to as the Vitamin B complex has been split up, on the basis of experimental reactions in animals, into no less than ten hypothetical factors concerning which very little is known.

All that can be claimed to date is that certain food substances appear to contain elements which are of use in the prevention and treatment of pellagra.

Many such substances contain protein of high biological value and B vitamins as they have in turn been defined, but these same food substances might be equally well looked upon as containing P.E.F., some

indeed might contain the anti-pellagra factor complete as will be mentioned later.

A complete withdrawal of P.P. factor from the diet should cause pellagra in all those so deprived according to GOLDBERGER's theory, but only six of the eleven convict volunteers of his experiment showed signs of the disease. As so often occurs in experimental work, the failures are left unexplained. Pellagra may occur in those who partake of a normal adequate diet. Their numbers are small it is true, as J. T. MARTIN (1931) pointed out, less than 4 per cent. of the cases of pellagra in the United States occur among the well-to-do classes. In endemic areas where pellagra has a high incidence, some members of a family develop pellagra, others are spared, though all live under the same conditions and take the same diet. R. FLINKER (1934) found that, in the Bukowina, pellagra broke out among those taking a good mixed diet and cleared up without any change of diet, and that the disease occurred in those who had lived for many years in endemic areas without change of conditions. He suggests the cause then lies in some digestive disturbance with achlorhydria. Pellagra will attack inmates of an asylum who have been living under unchanged conditions for years. A single extrinsic pellagra preventive factor will not account for such cases. Attempts have been made to explain some of these facts by supposing that there is malabsorption of the P.P. factor, but there is no evidence of this. The fact that substances containing P.P. factor will cure a condition produced by experimental deprivation of the same substances is no proof that P.P. factor will cure pellagra. R. H. TURNER (1931)* remarked that, in spite of special treatment based upon the knowledge gained by GOLDBERGER's work, death occurred in 25 per cent. of pellagrins admitted to the hospital in New Orleans in their first attack. F. P. UNDERHILL (1932) agrees: " Vitamin G therapy has made a poor show ! "

These and other facts lead to the conclusion that there may be a P.I.F. as well as a P.E.F.

T. R. BOGGS & P. PADGET (1932)* believe in the identity of Vitamin G on account of the results obtained with liver therapy. Of patients to whom liver was administered, 25 recovered and 7 died ; of those from whom liver was withheld, 26 recovered and 24 died. These figures, however, prove nothing about any particular vitamin. Forty of a series of one hundred and two cases were due to alcohol, and they suggest that alcohol destroys the P.P. factor in the gastro-intestinal tract, thereby preventing proper absorption.

G. A. WHEELER & W. H. SEBRELL (1932) had already shown that liver was rich in a pellagra-preventing factor.

BOGGS & PADGET found liver extract of no value in treatment ; on the other hand R. L. RAMSDELL & W. H. MAGNESS (1933) speak of the spectacular results obtained in 22 cases of pellagra treated with 2 cc. doses of liver extract No. 343 injected intramuscularly. The results of treatment will be referred to again later. So far, it is only fair to argue, from the results of treatment, that a number of food substances contain some one or more principles which are useful in treating the disease. The fact that particular liver extracts are of therapeutic use suggests that the anti-pellagra factor is stored in the liver. Two points may be emphasized here in attempting to evaluate any particular treatment. The first is, what signs shall be taken as evidence of improvement ; the second, how shall it be proved that the improvement is due to the treatment. As has already been mentioned,

the exanthem may clear up while the patient is progressing towards death. The exanthem and other symptoms may run a self-limited course and their retrogression be wrongly attributed to the particular treatment given.

To summarize this part of the argument: endemic pellagra is commonly associated with an ill-balanced diet deficient in substances containing protein of high biological value and the hypothetical P.P. factor (vitamin G), but this association is not invariable in either direction. Whatever the extrinsic factor may be, there is reason to believe that a second factor may be involved.

The evidence for postulating a second factor of the nature of an intrinsic factor, analogous to haemopoietin, and for believing that failure in its secretion is associated with chronic gastritis will now be discussed.

Practically all the causes of chronic gastritis, as put forward by Knud Faber (1935), figure in the history of pellagra including on the one hand noxious substances taken by mouth; alcohol, tea, coffee, curry and condiments, coarse vegetables, decomposed foods, associated in many cases with the habits of bolting food and overloading the stomach, and on the other hand causes of haematogenous origin: febrile diseases, acute and chronic infections, including among them pulmonary tuberculosis.

Zanetti (1778)* believed that bad food and bad water were aetiological agencies; sufferers from the disease were chiefly the very poor who could only afford the poorest food.

Gherardini (1780) also considered bad food, and especially bad maize, as the chief cause of the malady. Frapolli (1771)* added bad vegetables and called attention to the relationship of rancid butter and oils with pellagra. He found that the disease was particularly common in dyspeptics. Strambio (1789)* also alluded to bad food including maize and rancid oils and laid stress on all depressing influences.

W. X. Jansen (1788) remarked bad foods and mouldy cereals. L. Soler (1791) considered the disease to be due to inanition as the consequence of misery and filth. G. Cerri (1792) also referred to inanition. Thouvenel (1797) pointed out that pellagra was common in areas where the maize did not mature properly. F. L. Fanzago (1807) and G. B. Marzari (1810) were whole-hearted supporters of the maize theory followed, it should be remembered, by Guerreschi (1814), who believed a maize fungus to be the cause, and by L. Balardini (1845) who also urged mouldy maize as the chief aetiological factor in pellagra and T. Roussel (1845) who held the same view.

C. Lombroso (1870) in his well-known treatise maintained the causal relationship of bad maize to pellagra. J. B. Calmarza (1870) writing from Spain viewed pellagra as a disease produced by misery and alcohol. S. Nobili (1841) noted the abuse of wine, as others have done since. H. F. Harris (1919)* was convinced that dyspeptic disturbances played a big part and that mental anguish as noted since the time of Strambio was an important factor.

Thus we see mentioned in the observations of the older writers many of the more important aetiological factors in the production of chronic gastritis. All the theories which advocated some organism associated with maize as the specific cause of pellagra are, it is here suggested, no more than evidence of the use of bad grain. Such were the *Bacterium maydis*, Majocchi (1881); *aspergillus*, Ceni (1902);

streptothrix, Fossati, (1904); *streptobacillus*, Tizzoni, (1908); etc. The Illinois State Commission came to the conclusion that the disease was due to an infection unknown, but these and the more recent theories of infection, such as those of J. W. JOBLING and L. ARNOLD (1923), a fluorescent fungus of the aspergillus glaucus-repens group, of W. SUSMAN (1927) and of B. R. TUCKER (1935) who suggested a virus, fail to explain the facts and have received no support.

Specific maize theories, in one form or another, held the field over a very long period but it is worthy of note that maize was eaten in the endemic areas of Italy for the most part in the form of " polenta," referred to by many writers as a badly prepared and ill-cooked dish. In other areas maize meal was made up into an unleavened heavy acid bread. In more recent times a similarly indigestible diet was to be found in the endemic areas of the United States—corn-mush which is practically identical with polenta, corn-bread and hoecake, which are never properly cooked, salted hog-meat, pork fat and molasses.

In these facts we see potent factors in the causation of gastritis, which come into play with greatest intensity during the winter months. Thus may be explained the seasonal incidence of the dyspeptic symptoms which have been so commonly elicited in the histories of pellagrins.

Despite ALPAGO-NOVELLO's (1894)* naive remark—" One thing which has infinitely displeased me is to read in a certain report that some individuals presenting evident symptoms of pellagra did not use maize " and such *ex cathedra* statements as that made by H. B. DAY (1930) who said " Pellagra stands to maize as beri-beri to rice," the time has arrived when pellagra should be freed from the maize millstone which has hung about its neck for so many years. The eating of maize by white races has connoted poverty and, it is here suggested, nothing else. The theories which postulated maize as the one specific cause of pellagra fell to the ground in 1910 when H. S. STANNUS (1912; 1913)* demonstrated an outbreak of classical pellagra among central African natives living on a diet of rice and beans. Yet H. F. HARRIS (1919)* referring to these observations in his monograph refused to believe the facts as they did not fit in with the maize theory of which he was a staunch advocate. Even as lately as 1932 Miss H. CHICK (1933) in the Lamar Lecture, still upheld the old maize theory and went so far as to suggest that " the toxic substance in maize is transferred to corn-whisky " in order to account for the cases of alcoholic pellagra in America, while ignoring the fact that other forms of alcohol may appear as aetiological factors in the disease. Alcohol acts as a potent cause of gastritis, as a cause of pellagra it will be discussed later.

No one of those who have upheld any of the maize theories has ever offered any explanation of the fact that among many native races, whose stable diet is maize, pellagra is absent or very rare. The reason is obvious if the methods of preparation of these foodstuffs by natives be studied. The preparation of flour from maize by natives is a most elaborate and laborious process, carefully carried out, the final product being free from those qualities which have been adversely criticized in polenta. The same is true of other native flours such as that made from cassava. If, on the other hand, some ill-prepared maize product be given to children, such as was the case in the disease described by Miss C. WILLIAMS (1933, 1935)* one would expect severe gastritis to result. The same would be true of children fed on cassava food mentioned by D. G. Fitzgerald MOORE (1934)*. Even a change from

native-prepared maize flour to steam-milled maize will cause gastro-intestinal upset in natives; this being probably the explanation of the outbreak (of pellagra) in Northern Rhodesia described by P. A. NIGHTINGALE (1912)* as Zeism.

The part played by infections is suggested by a large number of observations. BABES (1910) remarked syphilis and malaria as predisposing causes; the French had noted the association of pellagra with any disease producing cachexia.

In warmer climates parasitic infestations play an even more important part. F. M. SANDWITH (1898)* and others have called attention to the association of pellagra in Egypt with hookworm infections. LONG (1910) put forward a pellagra theory based on the high incidence of amoebic infections in his cases. A. FAKHRY (1932)* showed that 92·3 per cent. of 178 pellagrins attending the ankylostome hospital in Cairo, were infected with *Schistosoma mansoni*, this being double the incidence of the infection in non-pellagrins. A. G. BIGGAM and P. GHALIOUNGUI (1933)* found bowel parasites in 24 of 25 cases investigated. Helminth, flagellate and chronic dysenteric infections were common among the Turkish prisoners of war before referred to. They were common in the Nyasaland cases. All these infections, it is here suggested, are common causes of chronic gastritis in native races, and therefore of aetiological significance when the other factors in causation come into play.

Some elements common in native dietaries may also play a part, such as salt-fish, highly seasoned and spiced foods, some oils, sour dishes, vinegar, etc., possibly tea and coffee, as noted in the histories of outbreaks of pellagra and pellagra-like conditions in Africa and in the East. Sugar-cane products may also possibly be incriminated. R. BLOSSER (1915) remarked that pellagrins recovered after cane-sugar, syrup and molasses, commonly taken in considerable quantities, were excluded from the diet. The central neuritis described by H. H. SCOTT (1918) in Jamaica was associated with an almost exclusive diet of cane. There is also the interesting fact in experimental work recorded by V. R. LEADER (1930). He found it was impossible to produce the pellagra-like condition in rats by special feeding if cane-sugar were excluded from the diet, and that the addition of cane-sugar to the deficient diet precipitated the onset of the condition. AYKROYD on the other hand succeeded but it should be noted that the corn starch which was used had been dextrinized by boiling.

All the several causes of chronic gastritis therefore figure commonly in the histories of pellagrins in all parts of the world. As HARRIS has emphasized, practically all pellagrins give a history of dyspepsia, and as HENNING says "Every dyspeptic suffers from gastritis."

One of the commonest results of chronic gastritis is failure in the secretion of hydrochloric acid. Hypochlorhydria occurs in a very large percentage of cases of pellagra and complete anacidity in the majority. The condition was first observed by LOMBROSO.

One or two points in the relationship of pellagra to achlorhydria are worthy of note. In an ordinary population failure in acid secretion is progressively more common in each successive decade, it occurs in a greater proportion of females and at an earlier age in that sex, and gastric acidity is lowered during pregnancy. The higher incidence of pellagra in the female has often been remarked and that it attacks women at an earlier age has been known since the time of CALDERINI (1844). That women were liable to develop pellagra during lactation

was first noted by STRAMBIO, while ALDALLI called attention to woman's susceptibility to the disease at the menopause.

Chronic gastritis with resulting failure of gastric acid secretion and achylia gastrica may not be uncommon among native races as shown by C. D. de LANGEN (1932–3) in the Dutch East Indies and yet pellagra is rare among them just as is pernicious anaemia. DE LANGEN had seen no case of the latter in Batavia and it will be recalled that no case was forthcoming when Miss L. WILLS (1935) was working on anaemia in Bombay.

On the other hand, as is true of beriberi and scurvy, pellagra and pellagra-like conditions appear prone to attack natives when confined in institutions, witness the outbreaks in the prisons of Africa, Malaya, etc., referred to in a previous article, facts which suggest that the metabolic equilibrium of these peoples is unstable. The added stress of manual labour with fatigue and mental depression may well be "the last straw" in upsetting the balance and precipitating an attack of pellagra, as was noted by the older writers ZANETTI, ODOARDI, ALBERA and STRAMBIO.

To H. DUDGEON of Egypt is attributed the saying " once a pellagrin always a pellagrin." He considers that pellagra is not caused by a specific dietetic deficiency, that while the latent pellagrin may be maintained in health on a sufficient diet, any defect in diet or failure in health will be followed by the development of symptoms of the disease. Others recognizing the same fact have spoken of a pellagrous diathesis ; but are such cases anything more than examples of unstable equilibrium ? Others have remarked the effect of an operation with ether anaesthesia or the exhibition of a purge in precipitating the attack of pellagra. N. L. CORKILL's (1934)* observations concerning snake-bite in producing an attack of pellagra have a similar bearing. These exciting causes may determine the extinction of an already failing secretion of a P.I.F.

The anaemia associated with pellagra is irregular in incidence. So far as published records go, no direct relationship has been established between the degree of anaemia and the severity of the disease, nor between the occurrence of anaemia and achylia or diarrhoea. We may recall in this connexion the fact that, as has been already mentioned, the condition may follow certain operations on the stomach.

The anaemia is also irregular in type—in most cases it is of moderate degree but it may be slight or marked, hypochromic or hyperchromic, with a varying colour index. The administration of any one specific therapeutic agent does not give uniform results.

The resemblances between pellagra and the hypochromic anaemia of Witts are of interest. In the latter, with an incidence chiefly in women of middle age, there are associated an atrophy and aphthous inflammation of the mucous membrane of the tongue and pharynx, cracks at the angles of the mouth, trophic changes of the skin, nails and hair, fatiguability and not uncommonly diarrhoea, together with hypochlorhydria, achlorhydria or achylia, but haemopoietin is present.

In pellagra it was assumed that Castle's intrinsic factor was being secreted by the stomach. This has been demonstrated by T. D. SPIES and W. PAYNE (1933) and confirmed by M. SALAH (1935) using Singer's method with rats.

It will now be of interest, in view of the hypothesis which has been suggested, to examine those groups of cases referred to by writers as

sporadic, pseudo-pellagra, para-pellagra, alcoholic and secondary pellagra.

Sporadic cases of pellagra were first noted nearly a hundred years ago; they gave rise to a considerable amount of discussion. BAILLARGER (1847) was the first to recognize a pellagrous eruption in a lunatic, but it was E. BILLOD (1859, 1865)* who proved how commonly pellagra affected the inmates of asylums. He referred to the affection as "Pellagra of the Insane." T. ROUSELL (1866) introduced the term "Pseudo-pellagra" and M. H. LANDOUZY (1860) included, under the term "Sporadic pellagra," all those cases which did not fit into the maize theory of the endemic disease. LOMBROSO (1870), BELMONDO (1889) and VEDRANI (1905) would not accept alcoholic cases as true pellagra, and L. MERK (1911) would not recognize those cases associated with alcoholism, cachexia, or psychopathy. H. F. HARRIS (1919) too, an ardent supporter of the maize theory, put forward the term "para-pellagra" to cover all those cases. He speaks of alcoholic pellagra, the pellagra of misery, the pellagra of the insane, and in a fourth group places all those "cases to which the term pellagra has been loosely applied, but which are evidently of an entirely alien character." He sweeps, into this side-track, cases which had been recorded in this country, including the well-known cases of C. R. BOX and the group of typical cases described by H. S. STANNUS in Central Africa.

Pellagroid was another term invented with no good reason; pellagroid is pellagra as V. H. GOUGEROT and J. MEYER (1932)* have pointed out.

Pellagra associated with alcoholism.

In the more northern of the United States where alcoholic pellagra has been a not uncommon affection in more recent years, it is now recognized by competent observers to be one and the same disease as ordinary pellagra; "Alcoholic pseudo-pellagra is an anachronism" exclaims one writer. With few exceptions the 71 male and 29 female pellagrins admitted to hospital in Philadelphia and reported by J. V. KLAUDER and N. W. WINKELMAN (1928) were alcoholic cases. They appeared to view the affection as an intoxication caused by alcohol. In the discussion of their paper J. F. SCHAMBERG suggested that alcohol acted by disturbing digestion, and E. D. CRUTCHFIELD referred to the difficulty of nourishing the alcoholic. Isolated alcoholic cases have been recorded elsewhere, by K. GRUNENBERG (1923) in Berlin, by L. ARZT (1926) in Austria, by OLIVER and FINNERUD (1927), F. C. KNOWLES & J. B. LUDY (1926), and others.

The history in these cases is well illustrated in a case described by C. W. FINNERUD (1929): a 32-year-old negress after taking 1 to 2 pints of "moonshine" a day for 6 weeks and nothing to eat, developed diarrhoea, nervousness, sore tongue and mouth, erythema on the backs of the hands, wrists and forearms, tremor and incoherent speech, with loss of weight. A dozen such cases are admitted annually to Cook County Hospital. They recover in from 2 to 4 weeks when put on a full diet.

E. R. MALONEY (1929) has published similar histories. He has referred to 21 cases of "alcoholic pseudo-pellagra." Symptoms appeared after 2 to 6 weeks' heavy drinking of "green whisky" with little more than a plate of soup and a crust in the day. Two of the twenty-one patients had delirium tremens, the rest had no mental symptoms; half were constipated, half suffered from diarrhoea. The exanthem

was seen on the hands, sometimes on the face, but in these cases never on the feet. Recovery occurred in from 8 to 12 days.

S. R. Mills (1934) has recorded twelve cases of pellagra with four deaths among seamen admitted to the Naval Hospital, League Island, Pa., following upon alcoholic debauches of several weeks' duration, when, beyond the boot-leg corn-whisky or synthetic gin, little had been taken by mouth except some oatmeal. In these cases the backs of the hands and wrists were the seat of the erythema ; the tongue and oral mucous membrane were red and raw ; diarrhoea was present and loss of weight had occurred; blood picture normal; achlorhydria present.

Of 14 cases admitted in seven years to the Boston Psychopathic Hospital under the care of R. H. Guthrie (1929) six were chronic alcoholics.

Gaté, P. Tiran and J. A. Thévenon (1932) mention the case of a 38-year-old French woman " bargee " with typical pellagrous affection of the skin, of the hands, wrists, fingers, face and of the mucous membrane of the mouth and vagina in which there was a history of chronic alcoholism but no dietetic restriction or monotony.

Perhaps the most interesting series of cases, especially in view of the effects of treatment, are those reported by T. D. Spies of Cleveland (1934, 1935). In a previous communication T. D. Spies and H. F. De Wolf (1933)* recorded the mortality among their pellagra cases as 54 per cent. when treated in hospital by care, diet and yeast. In the second series of 125 cases the mortality rate was reduced to 6 per cent. This was effected by even greater care in nursing in a special clinic, by scrupulous evaluation of the dietaries according to the needs of each case, by securing complete rest by means of sedatives and by the exhibition of one or more of the following preparations :

(*a*) Dry yeast powder, 75 to 100 gm. *per diem* by mouth.

(*b*) Liver extract 75 to 100 gm. *per diem* by mouth, or intravenously if necessary.

(*c*) Desiccated hog's-stomach 200 gm. as above.

(*d*) Wheat germ 250 to 300 gm.

Of these cases 95 per cent. had imbibed heavily and it was considered that the pellagra was secondary to failure of food ingestion. The symptoms found consisted in those of " central neuritis " : confusion, disorientation, hallucination, dementia, mania, which varied day by day, from hour to hour ; peripheral neuritis characterized by severe pain in feet, legs, and sometimes hands and arms ; anaemia in 60, per cent., of which a third showed a low colour index and two-thirds a high colour index ; erythema of skin and mucous membrane of mouth.

The authors add a note to the effect that " neurologic signs and symptoms of the two conditions (delirium tremens and pellagra following alcohol) are clinically indistinguishable in our series." Under the special treatment all symptoms respond, the skin lesions improve most rapidly, the symptoms of the central neuritis may recover after prolonged treatment, but it was not determined whether the peripheral neuritis was cured. A further interesting point and one of considerable importance was that 37 per cent. of cases relapsed when the treatment was discontinued.

The authors, as has been mentioned above, believed that pellagra supervened upon failure of food intake.

The facts, however, may be interpreted otherwise it is here suggested. Firstly, simple starvation for a few weeks will not result in pellagra ; secondly, alcohol is perhaps one of the most potent agents in causing gastritis and achylia ; may it not be a potent agent in inhibiting the secretion of a P.I.F. ? In the acute alcoholism, such as is depicted by American writers, we should expect the inhibition of secretion of P.I.F. associated with complete withdrawal of P.E.F. to cause pellagra. The suppression of P.I.F. might be temporary or permanent. In the former case recovery would be possible, in the latter not possible. The results obtained by treatment as detailed above appear to add weight to this argument, the large doses of hog's stomach, liver extract, etc., would contain, according to the hypothesis put forward, considerable amounts of the anti-pellagra factor complete ; when these were discontinued many patients relapsed. In some cases of acute alcoholism and in other cases of chronic alcoholism the power to secrete P.I.F. may be permanently lost.

These cases of alcoholic pellagra therefore appear to throw light on the general problem.

Pellagra due to voluntary restriction of diet.

S. A. Munford (1930) records the case of a 38-year-old woman, who following a faddist cult, lived on raw carrot, beef, artichoke, celery, lettuce, grapefruit, alligator pears, and crackers [biscuits] for four months and then for two months on a still more restricted diet. She developed dermatitis, diarrhoea, anaemia and mental apathy but recovered on forced feeding.

W. H. Mook and R. S. Weiss (1925) have reported the case of a 19-year-old girl, 6 ft. 1 in. tall, who, in order to reduce her weight, limited her diet to carbohydrate and some pork product. She came under observation weighing only 71 lb. The symptoms were red swollen tongue and gums, a glove dermatitis and pigmentation over the knees and elbows, loss of appetite, extreme atonia and diarrhoea. Gastric acid was present and there was no anaemia. Recovery took place on a protein diet. R. W. Brace (1929) cites a similar case, the diet consisted of carbohydrate, a little milk, little meat and no vegetable. P. S. Carley (1928) mentions the case of a 33-year-old woman who on account of indigestion and fear of cancer lived on practically nothing but cooked cereals. The pellagrous symptoms cleared up in two weeks with full diet and yeast. S. R. Roberts (1929)* notes a case of pellagra in a 64-year-old woman who for 40 years had taken an excess of candies [sweets], sweet preserves and bread, but no meat, milk or eggs and rarely vegetables.

The Danish labourer described by J. E. Holst (1935) who developed pellagra, but no gastro-intestinal disturbance and no achylia, on a diet of bread, margarine and coffee, is another example of sporadic pellagra due to dietetic restriction.

R. H. Guthrie (1930), A. E. Greer (1930) and N. P. Walker and G. A. Wheeler (1931), have witnessed the development of the pellagrous dermatitis in patients following a ketogenic diet. Seale Harris in the discussion on a paper by Dearman (1928) said he had seen pellagra develop in a tuberculous diabetic on a reduced diet but high in carbohydrate.

These would appear to be cases in which, according to the hypothesis here advocated, the disease depended entirely, or practically entirely,

on a deficiency of P.E.F., though in some of them there may well have been an associated gastritis with loss of P.I.F.

Pellagra in the Insane.

As is well known, pellagra may lead to insanity, the number of pellagrins in America who develop a psychosis being according to S. R. ROBERTS (1929)* about 10 per cent., but the insane are also prone to develop pellagra, as was realized in France long ago and in the United States since then, though the two facts have not always been clearly distinguished.

The point of interest, one to which attention is not called as a rule, is that only some of the inmates in any particular institution fall victims to pellagra. GOLDBERGER found that in certain asylums in the United States the number of lunatics developing pellagra each year was a constant proportion of the total.

He held that in the American institutions, prevention could be attained by giving foodstuffs such as protein, tomato juice or yeast vitamin in the form of Harris's Powder, a substance containing very little protein nitrogen. Inasmuch as Goldberger found them useful he spoke of them as containing P. P. factor, but this does not explain very much.

In this country before 1913, pellagra appears to have been unnoticed in our asylums. In the period 1913–1928 there were 108 deaths among asylum inmates. G. A. WATSON (1923)* reporting upon the cases at the Lancashire County Mental Hospital, Rainhill, stated that in some the disease was present on admission but that the majority of patients had been resident in the institution from six months to several years and one case for twenty-seven years. The majority were women between forty and fifty years of age. Of the diet it is stated that it was more generous and more varied, especially in regard to protein, in the year of the outbreak than in previous years. This, of course, is not synonymous with saying that a liberal amount of protein was ingested and absorbed. The age and sex incidence does, however, suggest that some disturbance of function was involved. May it not have been chronic gastritis, achlorhydria and a deficiency of P.I.F. ?

Gastric disturbances and gastritis are of course common in psychotics: it was noted by Watson at Cane Hill and more recently has been remarked by A. HOFMAN-BANG (1933) in all his pellagrins in Danish asylums.

Secondary Pellagra.

Fifty eight published cases of so-called secondary pellagra have been collected. Others may not have been recorded and some probably have escaped recognition. In nearly all, the disease has been associated with an organic lesion in the gastro-intestinal tract :—Oesophageal stricture, P. A. O'LEARY (1926) ; carcinoma of the cardiac orifice, F. W. ROLPH (1916) ; carcinoma of stomach, R. C. BRYAN (1919), BERON (1931), J. V. KLAUDER & N. W. WINKELMAN (1928) ; carcinoma of the pylorus, 2 cases, W. L. BENDER (1925), P. A. O'LEARY (1926), G. B. EUSTERMAN & P. A. O'LEARY (1931), S. TAKAHASHI (1929)* ; carcinoma of the alimentary tract, 4 cases, A. J. WYJASNOWSKY (1934)* ; pyloric ulcer, W. L. BENDER (1925), 2 cases, P. F. O'LEARY (1926) ; pyloric stenosis, A. MEYER (1932) ; duodenal ulcer, S. Levy SIMPSON (1935) ; operation for supposed

gastric ulcer, 3 cases, M. L. Graves (1920) ; duodenal feeding, 2 cases, W. C. Sandy (1919), 2 cases, T. E. H. Thaysen (1932)* ; gumma of stomach, R. H. Turner (1929) ; carcinoma of the head of the pancreas, I. Murray (1936) ; carcinoma of the lower ileum, 2 cases, F. R. Nuzum (1925) ; stricture of the jejunum and ileo-caecal valve, R. H. Turner (1929) ; tuberculous entero-colitis, R. W. B. Ellis (1930) ; tuberculosis of the bowel, O. R. Langworthy (1931), Yang & Hu (1930)* ; carcinoma of the transverse colon, A. R. Elliott (1927) ; carcinoma of the descending colon, P. A. O'Leary (1926) ; ulceration of the colon, Yang & Hu (1930)* ; colitis, J. M. Barnes (1925) ; poradenitic stricture of the rectum (Lymphogranuloma inguinale) 7 cases, E. von Haam & L. Lichtenstein (1935) ; rectal stricture (almost certainly of the same nature) 8 cases, R. H. Turner (1929) ; rectal ulceration and polyposis, Yang & Hu (1930)* ; recto-vaginal fistula, A. C. Lambert (1927)* (both also probably due to poradenitis) ; suppurating hydatid of the liver, C. E. Corlette (1924) ; multilobular cirrhosis of the liver, F. Lanzarini (1924) ; diaphragmatic hernia, M. B. Strauss (1934).

In many of the gastric cases cited operation was undertaken and in this regard they are of interest in that pernicious anaemia may similarly follow operation upon the stomach, the explanation lying, according to A. F. Hurst (1923), in the artificially induced gastritis and achylia. Similar cases, fifteen in number, are cited from the literature by R. A. Rolands and S. Levy Simpson (1932) who added two further cases of pernicious anaemia and subacute combined degeneration following gastrectomy and post-operative gastritis.

Pernicious anaemia may also be associated with stricture of the small intestine often tuberculous in nature, as reported by K. Faber (1895) and by A. F. Hurst (1933). The same association with stricture has also been noted by E. Meulengracht (1929), by J. C. Hawkesley & E. Meulengracht (1936) and by M. B. Strauss (1934) who has also seen pernicious anaemia develop after multiple intestinal anastomoses. Hurst has also referred to cases associated with simple or malignant strictures of the colon.

Rolands and Levy Simpson found that the anaemias developing after operations upon the stomach might be hyperchromic or hypochromic, that they bore no direct relationship with gastric acid secretion, the rate the stomach emptied, the presence of diarrhoea or the intestinal flora. S. J. Hartfall (1934) found that the degree of anaemia may be as marked after gastro-enterostomy as after partial gastrectomy, but that it is more common when the duodenum is occluded and gastro-jejunostomy has been performed.

These remarks apply in much the same way to the series of cases of secondary pellagra cited above, among whom anaemia also occurred in some proportion.

Hypochlorhydria, achlorhydria and achylia, deficient nourishment, vomiting, diarrhoea, operation upon the stomach and multiple anastomoses, continued duodenal tube feeding are all noted in the histories of these cases with varying incidence. No one of these factors is invariable and no exact generalization can be made.

The parallelism of these two series of cases is, however, worthy of remark and it is suggested that gastritis is the one common factor to all.

It would appear that in gastritis the stress of the pathological process may fall with unequal incidence upon the cells associated with the

secretion of a number of specific factors necessary to the normal metabolism of the body; in one case pernicious anaemia results, in another a hypochromic anaemia, in others subacute combined degeneration, pellagra, etc. In many cases more than one factor is involved and in a considerable proportion the secretion of hydrochloric acid is affected.

These cases of secondary pellagra appear to support the hypothesis that in pellagra there may be a default in an intrinsic factor.

Turning now to the pathogenesis of some of the symptoms in pellagra, the first to be discussed will be the dermatitis.

In a previous article the distribution of the exanthem in the attack of pellagra has been described. It was shown that the commonly accepted theory, which would explain the erythema as due to sunlight acting upon exposed areas of skin rendered sensitive by some photosensitizing toxin circulating in the blood, was untenable. Emphasis is again laid on this point as it is still the common habit to speak of pellagra as if light hypersensitivity were the one essential factor in the production of skin lesions.

The facts in regard to the distribution of the exanthem in pellagra may be stated, in reality, quite simply though they appear to have escaped the observation of most pellagrologists. The exanthem tends to appear in those areas of skin which, in any particular individual, have *undergone certain changes* as the result of the action *in the past* of traumata of various kinds including solar radiation, exposure to cold, friction, pressure, irritants, etc. This of course is true of the skin lesions in other diseases, as exemplified in variola, rosacea, etc., the distribution of the pigmentation in steatorrhoea will also be called to mind.

Sir Thomas Lewis in his monograph "The Blood Vessels of the Human Skin and their Responses" (1927) has shown that any noxious stimulus, of whatever kind, applied to the skin results in the liberation from the skin cells of what he called H-substance (since identified as histamine) which acts directly upon the minutest blood vessels of the skin in the neighbourhood and causes them to dilate. If the local concentration of histamine be large, stimulation of the sensory nerves may occur with the production, through the axon reflex, of dilatation of the larger arterioles. The release of histamine suddenly and in quantity, and especially if its action be prolonged, increases the permeability of the small vessels and if the damage be extreme rupture of these injured dilated vessels may occur with the production of a haemorrhagic reaction. If the reaction be less severe, as in ordinary sunburn, erythema, oedema and later desquamation and pigmentation occur. If the noxious stimulus be constantly repeated there results a permanent loss of tone in these smallest vessels with persisting dilatation and a heightening of the skin colour in the affected areas may occur.

Lewis points out that the areas of skin normally exhibiting this heightened colour are those uncovered according to the fashion of dress and therefore exposed to climatic variations. It has been demonstrated by counts made on the living subject that there is no fixed relationship between the actual *number* of blood vessels and the depth of the skin colour, but that on the other hand it varies directly with the *size* of the minute capillaries and venules. In the circumoral region, for instance, they are very small, whereas in the pink cheek and lobe of the ear they are much larger. The loss of tone and increase in

size of the minute vessels is progressive with age and is proportional to the degree of exposure, so that the gross enlargement may be seen not uncommonly in the skin of the cheeks and nose, on the backs of the hands and over a V-shaped area on the upper part of the chest in women in this country, sometimes with the formation of telangiectases.

The actual areas of skin which show these changes vary in different individuals, but as the result of long observations I think they may be written down definitely as the triangular areas of the cheeks, the bridge and sometimes the sides of the nose, the chin, the ears, some part of the forehead, the sides of the neck behind the sterno-mastoids with a prolongation up behind each ear and sometimes the neck in collarette-fashion with the V-shaped prolongation downwards over the sternum. The circumoral and circumocular regions and the throat are spared, though in some persons with a fullness between the eyebrow and eyelid this area is affected; in some also an area below the lower lid may be included. The backs of the hands, the forearms to some extent, the wrists bracelet-fashion and the shins may also be affected. All these areas which may suffer some degree of exposure are areas in which heightening of skin colour and telangiectasis may be observed. They are areas in which chapping occurs as the result of climatic exposure. This point is of importance; exposure to cold, wind, etc., is probably as potent a factor in causing these skin changes as sunlight, and the chapping of the wrists bracelet-fashion is worthy of note in connexion with the distribution of the exanthem in pellagra.

Noxious stimuli other than climatic exposure may produce similar results in the skin, tension, pressure, friction, any form of radiation, chemical irritants, etc.—well seen after exposure to X-rays, after prolonged exposure to heat and so on. The skin of the back of the hand in many people, as the part of the body probably most exposed to injury, shows very well the changes under discussion. Lewis has demonstrated that the venules of the skin over the knuckles have less tone than those of the skin of the back of the hand, and these in turn less than those of the skin of the forearm, etc., a point of great interest in view of the particular affection of the knuckles and backs of the hands in pellagra.

Anything which ordinarily causes flushing of the skin will cause an intensification of the colour in these "areas of heightened colour" as above described. When a general vasodilatation in the skin occurs it is only apparent as a rule in those areas of skin in which vascular tone has been lost, elsewhere it is "concealed or unrevealed." Lewis cites Darwin's observation that when the face and neck redden in blushing the whole body tingles and feels hot to the subject, a point of interest in connexion with "burning in the palms of the hands and soles of the feet," a symptom in pellagra referred to below.

An injection of histamine will induce flushing in isolated and distant parts of the skin which have suffered previous injury, thus illustrating the fact that differences of minute vessel tone may be concealed until sufficient strain is thrown upon them.

These facts suggest a possible explanation of the distribution and mechanism at work in the production of the acute exanthem in pellagra, namely that there may be liberated into the general blood stream at the time of the appearance of the exanthem some substance with a histamine-like action. While the general dilatation of minute blood vessels remains "unrevealed" the maximum effect would be witnessed in those areas of skin in which the blood vessels had lost their tone,

become dilated and permeable as the result of previous repeated traumata. The areas of skin affected in a classical case of pellagra correspond to those affected by exposure to climatic conditions. In the less common sites for the eruption similar changes may have been produced by noxious stimuli or trauma other than climatic exposure. Thus would be explained the affection of areas of skin liable to intertrigo, as beneath the breast and about the genitals; of the areas subjected to pressure such as the buttocks and knees; of the areas subject to friction about joints, over prominent veins, mucocutaneous junctions, etc. It would account for the bracelet-like involvement of the wrists, for the atypical distribution which may be seen in the infant, for the freedom of the face in veiled Turkish women and for the occurrence of the rash in typical distribution in those who have been bedridden for some long period. It would explain why the dermatitis of pellagra tends to appear each year, sometimes with ever increasing severity, at the same sites and also offer an explanation of the localization of the skin manifestations to the scrotum in the cases described by Landor & Pallister, all referred to in a previous article.

That the exanthem of pellagra is associated with the liberation of histamine there can be little doubt, that there is a general liberation of that substance into the blood stream seems unlikely. More probably what happens is a local liberation in areas of skin, already damaged as above mentioned, when some substance necessary for its normal metabolism falls below a given level.

This substance according to the hypothesis put forward is the antipellagra factor synthesized in the stomach. It is this interference with the normal metabolism of the skin which accounts for the fact that for some short period after the appearance of the dermatitis any part of the skin will react to a noxious stimulus with the production of a pellagra-like lesion but that later the same stimulus produces only a normal reaction.

A partial failure of this factor spread over a long period might give rise to the more chronic and more generalized skin changes already described.

The mechanism of the production of the affections of the mucous membranes as seen in the mouth, etc., is certainly of similar nature to that operating in the case of the skin, though this is not apparently generally recognized. The part played by the ingestion of hot condiments and rough food-stuffs, referred to by some writers, is not without interest in this connexion, as exciting cases of stomatitis in pellagra.

The diarrhoea, like the sialorrhoea, is secondary to the affection of the mucous membranes.

A number of references have already been made to the common symptom in pellagra—" burning of the soles of the feet and palms of the hands," and it has already been suggested on clinical grounds that this symptom is not a manifestation of a peripheral neuritis as has been commonly inferred by many writers.

Though this burning pain is most commonly remarked in the soles of the feet and less often in the palms of the hands, it may also be felt in areas of skin affected by the exanthem preceding or accompanying the erythema; more rarely it occurs in skin unaffected by the rash and may be felt all over the body. Burning pain, which would appear to be on an exact parallel, is again a common symptom referred to the mouth and pharynx, while a characteristic burning pain in the stomach is often complained of. This distribution again suggests that there is

some underlying general cause and that localization depends on some local condition. It would appear possible that it is the specialized texture and particular anatomical formation of the skin of these parts which determines the localization of the symptom to the palms and soles.

In both situations the skin has a special development to withstand pressure, both are endowed with a rich network of blood vessels, in both the areas of maximum pressure are areas of heightened colour. It might be expected that the exanthem in pellagra would find in them sites of predilection. Though, of course, both may be affected, as pointed out by the Pellagra Commission, Illinois (1911-12)* and as mentioned by HAMEAU long ago (1829)* it is a rare phenomenon and I would suggest that, while the special character of the skin in these situations hinders the appearance of the exanthem, it exaggerates the burning pain. The researches of LEWIS are again of great interest in this connexion. Under the title "Clinical Observations and Experiments relating to Burning Pain in the Extremities (1933, 1934)" he records observations showing that if the skin be damaged in any way it passes sooner or later into what he calls "the susceptible state" *i.e.*, a state in which pain recurs spontaneously and one in which the skin is hypersensitive and the threshold for heat is lowered. The original noxious stimulus may be of any kind including cold, heat and other forms of radiation.

This symptom, which Lewis refers to as erythalgia, was shown to be due to the action on the pain nerve endings of a naturally occurring substance released locally, presumably from the skin cells, like histamine but not histamine.

Any area of skin or mucous membrane may be affected with the "susceptible state." The common site for this pain is the sole of the foot, across the base of the toes, spreading to the remainder of the plantar surface, sometimes also to the dorsum of the foot and the ankle. The palms of the hands may be affected, also the legs and arms, the back of the neck, back and the V-shaped area on the chest, the malar regions and the brows, but elsewhere on the trunk the sensation is only one of warmth. That this same mechanism accounts for the burning sensations in pellagra there can be little doubt.

Of no less importance than the dermal and gastro-intestinal symptoms in pellagra are the nervous and mental manifestations. In the past the custom has been rather to think of the one in terms of degenerated cells and fibres and of the other merely as a cause for detention in an asylum. Here it is not proposed to discuss "the pathology of the dead-house," to use S. A. KINNIER WILSON's apt phrase, nor the chronic demented inmate of the institution. On the other hand one has only to watch carefully a case of acute pellagra to be struck by the fact that the nervous and mental symptoms often vary from day to day, from hour to hour, and that one is witnessing the signs of an acute physico-chemical disturbance in the balance of metabolism within the central nervous system. That the processes going on are "reversible" would seem apparent in view of their variation and quick response to treatment.

These symptoms have always been looked upon as toxic in origin but it would seem more probable that they are of the same order as those which occur in B_1 avitaminosis. Prof. R. PETERS (1936) has shown that vitamin B_1 in the form of "catatorulin" prepared from

yeast acts as a catalyst in the normal combustion of carbohydrate in the central nervous system of pigeons.

The clinical evidence in pellagra suggests that in a similar way the early acute nervous and mental manifestations may be due to the loss of some factor which acts as a catalyst in normal metabolism of nervous tissues—such a loss might be partial or complete, gradual or rapid, temporary or permanent, in this way accounting for the variation in the clinical picture.

The disturbances in function of the nervous tissues may depend upon a change in the normal dispersion of cell colloids in the direction of agglomeration or flocculation as is believed to occur in the manic-depressive psychoses by W. D. Bancroft & J. E. Rutzler, Jr. (1931) and H. B. Lang & John Paterson (1931).

So long as the process has not gone beyond a certain limit or persisted too long, it remains reversible and recovery is possible, otherwise permanent changes occur with symptoms of an organic lesion.

This hypothecated catalyst in pellagra is normally elaborated in the stomach, it is suggested, in an analogous manner to neuropoietin.

Whether the default of a single factor is responsible for the symptoms of pellagra seems uncertain, it is more probable that several factors are involved.

General Summary and Conclusions.

1. Pellagra has a world-wide distribution.
2. There are a number of conditions both in temperate and warm countries which resemble pellagra in that they present many of the symptoms of that disease though not exhibiting the classical triad of signs " Dermatitis, Diarrhoea, Dementia " without which, but quite wrongly, it has been commonly supposed a diagnosis cannot be made.
3. Many cases, without the endemic areas, go undiagnosed because the symptomatology of the affliction is not generally well recognized.
4. There are no separate conditions such as have been designated pseudo-pellagra, para-pellagra, alcoholic pellagra, secondary pellagra, pellagroid, etc. ; they are simply cases of pellagra.
5. Maize plays no specific part in the aetiology of the disease.
6. All the Theories of Causation which postulate a specific infective agent lack support.
7. Deficiency of Protein of High Biological value *per se* is not the cause of pellagra.
8. There is no definite evidence that pellagra is a simple avitaminosis.
9. A study of the disease from a wide angle suggests a new hypothesis namely that pellagra is one among a number of conditions which are severally due to a failure in the production of " principles " by the interaction of " extrinsic factor " in the food with " intrinsic factor " normally produced in the gastric juice.
10. In pellagra one or other or both factors may be involved, an extrinsic factor due to deficiencies in diet, an intrinsic factor due to non-secretion consequent upon gastritis.
11. The extrinsic factor is commonly present in foodstuffs containing protein of high biological value and some parts of the Vitamin B complex.

12. The anti-pellagra factor is probably stored in the liver. Refined liver extracts advocated for the treatment of pernicious anaemia should not be used for pellagra.

13. Its action is probably that of a catalyst, governing the metabolism of the cells of the skin, mucous membranes and nervous system.

14. What has been spoken of as the anti-pellagra factor may be really a complex of separate factors.

15. The distribution of the exanthem in pellagra is determined by pre-existing changes in the skin due to traumata of many kinds.

16. The changes in the tissue cells are of the nature of a change in the colloid state of their contents towards lessened dispersion of flocculation.

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MALARIA.

Bulletin de la Société Médico-Chirurgicale de l'Indochine. 1936. June. Vol. 14. No. 6. pp. 486–679.—Premier voyage international d'études malariologiques de la S.D.N. en Indochine. [**First International Study Tour of Malaria in Indo-China under the League of Nations.**]

This issue of the Bulletin contains twenty-seven papers dealing with almost every aspect of the malaria problem of French Indo-China, prepared, in the first place, for the benefit of the participants in the third International Course of Malariology, organized by the Eastern Bureau of the Health Organisation of the League of Nations, in Singapore. A three weeks' tour in Indo-China followed the six weeks' theoretical and practical laboratory course that was held in Singapore. Together these papers give a very complete picture of present malaria conditions in Indo-China and afford striking evidence of the greatly increased effort in this field that has characterized the last five years.

The following 18 papers call for special notice :

Farinaud (M. E.) & Moreau (P.). Principes et technique de l'enquête malariologique en Indochine. [**The Principles and Technique of Malaria Investigation in Indo-China.**]—(pp. 488–497. With 1 folding map & 1 folding plan.)

The principles underlying malaria surveys and the technique employed in carrying them out are well outlined. Both are familiar to all workers in this field. A chart shows in graphic form the geographical distribution of the various organizations and agencies collaborating in the campaign now being waged against malaria in Indo-China.

Farinaud (M. E.). Développement de la lutte contre le paludisme sur les plantations du sud de l'Indochine. [**Development of the Anti-Malaria Campaign in the Plantations of South Indo-China.**]—(pp. 498–514.)

This contribution reminds the reader that malaria has been a serious cause of suffering and death in Indo-China since the most remote times and that the " human geography " of the country has been determined in large part by the geographical distribution of malaria. In certain coastal areas malaria is a seasonal disease. As soon as one approaches hilly country in the hinterland malaria is found to be endemic and is a serious obstacle to the economic development of the country. Any unusual movements of population are likely to give rise to explosive epidemics. In the history of the development of rubber plantations malaria has been a vital problem from the beginning. The red-soil districts are specially suitable for rubber plantations. These were very scarcely populated but as soon as forest began to be cleared by imported Annamite labour trouble began. The situation was very critical in 1927–28. In some areas deaths amounted to 400 per thousand of the labour force : deaths, desertions and repatriations resulted in the loss to certain companies of 55 per cent. of their labour forces in 18 months. In 1929 Morin reorganized the campaign. It was shown that *A. minimus* was the most important vector as it is indeed throughout Indo-China. Drainage and oiling were largely extended. Subsoil drainage is complicated by the very unequal distribution of the rainfall

in Southern Indo-China. The average annual rainfall is 2,010 mm., of which 3 mm. falls in January, 337 mm. in September. Falls of 150 mm. in a single day, or in a few hours, are not unknown. Preventive quinine has been largely used. Adult mosquitoes have been attacked by fumigations. Encampments have been built as far as possible from mosquito breeding places and from the villages of the aborigines, of which from 80 to 90 per cent. were found to be infected. The elimination of mosquito breeding by shade plants has been tried, as has flushing. More recently atebrine and plasmoquine (or rather the French manufactured equivalents, quinacrine and praequine) have been used with success. Finally, much attention has been given to general sanitation. As a result of all this it has been possible, nearly everywhere, to control epidemic explosions, to reduce the death rates, and to keep the daily sick rates below 5 per cent. In 1900 the production of rubber in Indo-China amounted to 340 tons ; in 1935 to 30,000 tons.

Fabry. Thérapeutique clinique du paludisme. [**Clinical Therapeutics of Malaria.**]—(pp. 515–523.)

An admirable lecture on the treatment of malaria by a physician who has evidently very wide experience. In the treatment of the attack Dr. Fabry considers that quinine and atebrin have equal value in benign tertian infections, but in severe malignant tertian infections, such as are met with in Indo-China, atebrin is definitely superior to quinine. The treatment of chronic malaria is well handled. The human organism itself and time are the most important factors in recovery and every care should be taken not to damage the former. " Peu de thérapeutiques exigent autant de l'artiste que doit être le médecin."

Dorolle (P.). Inconvénients et dangers de la malariathérapie dans un pays d'endémicité malarique. [**Difficulties and Dangers of Malaria-Therapy in a Country where Malaria is Endemic.**]—(pp. 524–532.)

Dr. Dorolle has not had a fortunate experience in Indo-China in the treatment of general paralysis by malaria-therapy. Only *P. vivax* has been used : the local strains of *falciparum* are apt to be too virulent. Infection was given by the subcutaneous injection of infected blood. In many patients there were little or no signs of infection, owing to the patients' immunity, and rarely enough febrile reaction to confer any benefit. In other cases the injection lit up latent infections of malignant tertian or quartan malaria, which were very severe and difficult to cure. Small epidemics of malaria in the neighbourhood of the hospital that were attributed to malaria therapy also occurred. Dr. Dorolle's experience has led him to abandon malaria therapy : in its stead he now uses intravenous injections of dead microbial emulsions.

Canet (J.). Prophylaxie collective par médicaments synthétiques sur les plantations des terres-rouges (1934–1936). [**Prevention of Malaria by the Administration of Synthetic Drugs in the Rubber Plantations.**] —(pp. 533–559.)

In the malarious rubber plantations of Indo-China the incidence of the disease is high throughout the year but the months of maximum intensity are those which precede and follow the rainy season, that is to say June to August and December to the middle of March. The mass distribution of quinine during these months has proved to be of very limited value. Synthetic drugs have given better results, more

especially the association of quinacrine with praequine. The dosage and other details of treatment have varied according to circumstances. Though the benefits conferred by this "preventive" treatment are very real they are rapidly lost when treatment ceases: continuous treatment is obviously not practicable. A combination of anti-larva prophylaxis and mass treatment with synthetic remedies should, however, produce a permanent improvement in the health conditions of the plantations.

Canet (J.). Organisation de l'hygiène sur les plantations des terres-rouges. [**Organization of Health Activity in Rubber Plantations.**]—(pp. 560–571.)

An account of the general sanitary and health measures that have been applied during recent years to improve the lot of the labour forces on plantations.

Moreau (P.). Le paludisme au Cambodge. [**Malaria in Cambodia.**]—(pp. 582–586. With 1 coloured plan.)

Cambodia has suffered from malaria from time immemorial. The control of malaria is still the outstanding problem in connexion with the economic development of the country. The indigenous population is highly immune but possesses a very limited capacity for work. The spleen index is higher than the parasite index. The central part of the Province is relatively free from the disease: this is the region of the great lakes. There are parts of the coast where salt-water breeding anophelines, notably *A. ludlowi* (*sundaicus*) convey infection, but the most malarious districts are in the neighbourhood of the hills and of the stony outcrops so characteristic of the country. Here *A. minimus* is the chief vector; other vectors in the order of their importance are *maculatus*, *aconitus* and *jeyporiensis*. Larvae of *umbrosus* have also been found. Cambodia is a country of hyperendemic malaria.

Simon & Darbes. Résumé des progrès réalisés à Phnom-Penh dans le domaine de l'urbanisme et de l'assainissement. [**Sanitary Improvements in Phnom-Penh.**]—(pp. 587–592.)

A record of progress during recent years in the modernization and sanitation of Phnom-Penh, the capital of Cambodia. It is an important river port. Its sanitary problems are complicated by the fact that for several months of the year the water in the river rises well above the level of the drains of the town.

Souchard (L.). L'Institut Pasteur de Dalat. [**The Pasteur Institute at Dalat.**]—(p. 593.)

The fourth Pasteur Institute of Indo-China was opened in 1936 in Dalat, a hill station in the south. Apart from routine and research work connected with local health problems its major preoccupation is the manufacture and distribution of bacterial vaccines.

Yersin. Note sur les essais d'acclimatation des quinquinas entrepris en Indochine par l'Institut Pasteur. [**Attempts at acclimatizing Cinchona in Indo-China.**]—(pp. 594–595.)

Dr. Yersin, whose name will always be associated with the discovery of the plague bacillus, has been very active in his attempts to acclimatize cinchona in the hilly country of South Annam, at an elevation of about 3,000 feet. The young trees grow very well for a time; they flower and fruit very early, however, which probably indicates a short life. In the fourth year disease begins to attack the trees. The

culture is still in the experimental stage and there is still reason to hope for results that will not be unsatisfactory from the economic point of view.

Le Nestour. Protection antimalarienne des chantiers de constructions du chemin de fer de Tourane à Nha-trang (région du Varella). [**Protection against Malaria of the Labour Forces engaged in the Construction of the Tourane-Nha-trang Railway.**]—(pp. 609–611.)

The last section of the Trans-Indo-China Railway is approaching completion. It runs from Tourane to Nha-trang, two towns on the southern half of the long coast line of Annam. Its construction has entailed piercing Mont Varella, which is so picturesque a landmark on the coast : there are seven tunnels, the longest being 1,175 metres. The task of protecting the labour forces engaged on the work from malaria has called for much care ; this force has averaged 2,400 workers. The country is highly malarious. That considerable success attended the efforts is evidenced by the fact that in 1934 the deaths from malaria did not exceed 26. In 1935, however, the death rate was higher ; there were 17 deaths attributed to malaria cachexia.

Antoine (M.). Prophylaxie rurale du paludisme par irrigation alternée des rizières. [**Prevention of Rural Malaria by Intermittent Irrigation of Ricefields.**]—(pp. 612–615.)

This is an interesting account of an attempt to control rural mosquito breeding by the intermittent irrigation of rice-fields. If a ricefield be irrigated for three days in six it is dry for twenty-four hours once in six days. This procedure eliminated all mosquito breeding and the crop did as well as that of control rice-fields irrigated in the usual way. Inquiry is still going on with the object of determining the minimum amount of water that is compatible with a good yield.

Deniel. Rapport sur l'extraction de la quinine et des alcaloïdes totaux des écorces de quinquina de provenance Indochine. [**Method employed in the Extraction of Quinine and of the Total Alkaloids of Cinchona from Locally Grown Bark.**]—(pp. 616–618.)

A description of the method employed for the extraction of quinine and of the total alkaloids of cinchona from locally grown bark. The bark in 1936 yielded on the average quinine sulphate 3·5 per cent. ; total alkaloids 7·4 per cent.

Le Nestour. Le paludisme en Annam. [**Malaria in Annam.**]—(pp. 619–624.)

Annam is a long strip of land between the sea and high mountains that is everywhere cut up by isolated hills or off-shoots from the higher range. Such flat country as there is is very densely populated. Wherever there are hills there is very severe malaria, and in the foothills malaria is a killing disease. Years of great dryness are bad malaria years. Normally, violent storms are of frequent occurrence in the dry season which is the malaria season ; these storms are useful as they flush the anopheline breeding places. If crops fail the situation is aggravated by undernourishment of the population. The anophelines found are *minimus*, *maculatus*, *jeyporiensis* and *aconitus*.

Vaucel (M.). Le service antipaludique du secteur Nord-Indochine. [**The Anti-Malaria Service of North Indo-China.**]—(pp. 625–630.)

The antimalaria service of the Pasteur Institute at Hanoi was created in 1931. The report gives a summarized account of the

surveys carried out and the work accomplished by the Service since its creation.

The northern part of Indo-China consists of (1) the low lying deltaic region, (2) a belt of land between the former, and (3) the Middle Region with numerous water courses ; and (4) a high mountainous region with large valleys and deep ravines. In areas 1 and 2 malaria occurs but is not a serious disease : here *A. sinensis* and *A. vagus* predominate, neither being very efficient vectors. In areas 3 and 4 malaria is a deadly disease : here *A. minimus*, *A. jeyporiensis* and *A. maculatus* prevail.

Gaschen (H.). Les indices maxillaires des anophèles. [**Maxillary Indices of Anopheles.**]—(pp. 631–636. With 6 figs. & 1 chart.)

Previous papers by Gaschen on the maxillary indices of Anopheles have been summarized in this *Bulletin*. This communication refers to the work that has been done and gives an interesting account of the technique employed in counting the teeth and of the difficulties that may be experienced. As a criterion of "pathogenicity" of anophelines the maxillary index is not absolute but its determination is of use in a study of the feeding proclivities of these mosquitoes. The maxillary indices of the zoophile species *hyrcanus* var. *sinensis* and *vagus* are given as 15·7 and 14·2. The malaria vectors have indices as follows : *minimus* 11·3, *aconitus* 11·5, *maculatus* 11·4 and *jeyporiensis* 11·9.

Moreau (P.). Le paludisme dans l'armée en Indochine. [**Malaria in the Army in Indo-China.**]—(pp. 647–656.)

Malaria has ever been one of the most formidable enemies that the army has had to face in Indo-China. The difficulties have been very great in outlying posts in the high mountainous region in the north, part of which lies along the frontier of China. Here again *A. minimus* is responsible for most of the trouble. Recently antilarval measures near outlying posts, large permanent drainage work in rural centres in the high regions, mass treatment with quinacrine and praequine, the rational utilization of locally raised troops and general attention to the soldiers' well-being have effected a marked improvement.

Gaschen (H.) & Marneffe (H.). Le rôle des vecteurs dits secondaires. [**The Rôle of Anopheline Vectors of Secondary Importance.**]—(pp. 665–669.)

An interesting discussion of anophelines of secondary importance as transmitters of malaria. The authors call attention to the interesting fact that certain species that play a capital rôle as vectors of malaria in some countries are almost innocuous in others. Examples are given. *A. hyrcanus* var. *sinensis*, an important vector in China and Formosa, is of little account in Indo-China, as a rule, in spite of its prevalence. Recently, however, it was found to be the chief vector in a small localized outbreak in the delta of the Red River, so it is potentially dangerous even in Indo-China. Previously only one infected *sinensis* had been found in Tonkin. Similarly neither *aconitus*, *vagus* nor *maculatus* are of much importance in Indo-China. *A. culicifacies* occurs; one infected specimen was found. Its relative infrequence may be sufficient to explain its local unimportance as a vector.

The remaining nine papers are here noted in title only.

Cros (M.). Note au sujet de l'assainissement antimalarien des centres de Hon-quan et Budop (Province de Thu-dau-mot). [**Note on the Successful Anti-Malaria Measures applied in the Administrative Centres of Hon-quan and Budop.**]—(pp. 572–574.)

Gerber (M. R.). Budop. Un exemple de sanitation rurale. [**Budop. An Example of Rural Sanitation.**]—(pp. 575–578. With 1 map.)

Combaudon (E.). L'assainissement de la plantation de Snoul. [**Sanitary Improvements in the Snoul Plantation.**]—(pp. 579–581.)

Jacotot (H.). Les protozoaires sanguicoles du bétail et de diverses espèces animales de l'Indochine. [**Protozoa in the Blood of Cattle and Other Animals in Indo-China.**]—(pp. 596–604.)

Tregouet. La léproserie de Qui-hoa. [**The Leper Asylum of Qui-hoa.**] —(pp. 605–608.)

Farinaud & Moreau. Tuyên-quang. L'assainissement d'un centre de la Moyenne-Région Tonkinoise. Travaux permanents. [**Sanitary Improvements in Tuyen-quang, a Malarious Station in Tonking.**] —(pp. 637–646. With 1 folding plan & 1 folding chart.)

Marneffe (H.) & Gaschen (H.). Le paludisme côtier dans la région des lais de mer. [**Coastal Malaria in the Area of Reclaimed Land.**] —(pp. 657–661.)

Raynal (J.), Vaucel (M.) & Hoang-Tich-Try. La réaction de Henry en Indochine. [**Henry's Reaction in Indo-China.**]—(pp. 662–664.)

Gaschen (H.). La faune anophelienne du Tonkin. [**The Anopheline Fauna of Tonking.**]—(pp. 670–679.)

Norman White.

Bengal, Govt. of: Public Health Department. **Report of the Bengal Field Malaria Research Laboratory at Krishnagar for the Years 1929–1932** [Sur (P.), Assistant to Assistant Director of Public Health].—32 pp. With 14 charts. 1936. Bengal Govt. Press, Alipore.

The Krishnagar Field Laboratory was established in 1926 to study conditions in a hyperendemic malaria region of Bengal. A report on the observations made during the first three years was published in 1929; the present report is concerned with the work done during the four years 1929–1932. The Laboratory was closed down in 1932.

All anopheline breeding places in four villages were examined twice a month. Of the 79,398 larvae caught 53·1 per cent. were *subpictus* or *vagus*, 14·1 *barbirostris*, 10·8 *hyrcanus*, 9·3 *annularis*, 5·5 *philippinensis*, and 5·4 per cent. *pallidus*. The remaining larvae were *ramsayi*, *aconitus* or *varuna*, *tessellatus* and *culicifacies*.

Of adult mosquitoes caught in cattle sheds the most prevalent species were *annularis*, *subpictus*, *pallidus* and *vagus*. In dwelling houses the same species were chiefly in evidence, but here *philippinensis* was also quite numerous.

The only species found naturally infected in any numbers was *philippinensis*: of 2,902 dissected during the last two years the sporozoite infection rate was 2·1 per cent., the highest monthly rate being 5·3. This species is considered to be the most important vector in this part of the Nadia District.

Of the positive blood films examined 1,218 were identified as *vivax*, 1,002 *falciparum* and 975 *malariae*, a very high proportion of quartan fever. *N. W.*

Mira (Mario Giaquinto). La malaria en Guatemala. Estudios epidemiológicos y desarrollo de la campaña antipalúdica. [**Malaria in Guatemala. Epidemiological Studies and Development of the Antimalaria Campaign.**]—54 pp. With 1 map, 4 figs. & 3 graphs. Edizioni "Rivista di Malariologia." 1936. Rome: Stamperia Moderna S.A., Via Germanico, 136.

This report summarizes the results of six years' intensive work in the investigation of malaria conditions, and in the control of malaria, that has been carried out by the special department of the General Direction of Public Health of the Government of the Republic of Guatemala. It is not possible to summarize in small space the information contained in a report of 54 pages which is itself but a résumé. All that can be done is to direct attention to certain points of interest.

Guatemala has a population of two million; it covers 109,000 square kilometres of most diversified country—hot, moist, tropical coastal areas bordering the Pacific and the Atlantic; high mountainous tracts and volcanoes; extensive plateaux and plains; deep valleys and numerous rivers. The twenty-two departments into which the country is divided have very diverse climatic and other conditions: the one characteristic which they all, with but one exception, appear to have in common is the prevalence of endemic or hyperendemic malaria. Malaria is the big social and economic problem of Guatemala; the future progress and prosperity of the country is intimately bound up with the solution of that problem. That this statement is no exaggeration, facts and figures reproduced in the report amply testify. This is no new problem: malaria has been the scourge of the country from time immemorial. It was only in 1929, however, that a special malaria organization was created by the Government, with laboratory and other equipment, and an ambitious programme, on lines laid down by the League of Nations Health Organisation's International Malaria Conference of 1928.

It is evident that the successful prosecution of an antimalaria campaign in a country with such a variety of geographical, climatological and ethnographic conditions necessitates preliminary comprehensive malaria surveys. Such surveys have occupied much of the attention of the organization. These have embraced the study of morbidity and mortality data, the determination of splenic and parasite indexes, a study of the anopheline fauna and other factors concerned with the delimitation of endemic zones. In various regions local experimental methods of control have been studied. An investigation of the quinine requirements of the country is being made. Lastly, new legislation is being prepared which will provide for the organization of services charged with the treatment and prevention of malaria throughout the country.

The anopheline fauna is rich. *A. albimanus* is considered to be the most important vector; it is very widely distributed. Though it prefers tropical humid conditions such as exist on the shores of the Atlantic and the Pacific, it adapts itself to hot dry regions as also to the very different conditions prevailing at altitudes of from 1,000 to 1,100 metres, and even higher. In such places, however, its prevalence is not excessive. *A. albimanus* is the most prevalent species in all parts

of the country in which *falciparum* infections are most in evidence. *A. pseudopunctipennis* is also very widely distributed. It has a preference for high altitudes—500 to 800 metres. It is the predominant species in many areas of intense malaria and appears to be most efficient as a vector of *vivax* infections. *A. argyritarsis* cannot be excluded as a vector in certain localities. *A. hectoris* has been found at altitudes of from 1,300 to 1,550 metres ; laboratory experiment has shown it to be a potential vector, but its practical importance has not been determined. *A. vestitipennis, A. apicimacula* and *A. eiseni* all occur but are probably of little importance.

In the country as a whole *vivax* infections are the most widely diffused; they predominate in all high areas and also in many places little above sea-level. There are localities, mostly low-lying, where *falciparum* infections occur exclusively and many in which they contribute from 25 to 35 per cent. of the total infections. In certain isolated localities quartan infections are very prevalent ; there are places in the valley of the Polochic River where 28 per cent. of the positive blood findings were quartan. Mention is made of the high percentage of positive blood films in which gametes were found.

A brief description is given of several malaria control experiments that have been carried out with encouraging results. For example, in Puerto Barrios in 1929 the spleen index was 81·4, the parasite index 38·6 ; in 1931 they were 58·4 and 16·2, respectively. In Nueva Santa Rosa spleen and parasite indexes of 100 and 38·1 were reduced to 78·3 and 10·2 in the same two years, and in Monjas from 97·5 and 50·5 to 55·1 and 20·2. *N. W.*

WHITE (R. Senior). **Williamson's " Herbage Cover " Method of Larval Control. A Preliminary Note on Some Field Trials.**—*Records of the Malaria Survey of India.* 1936. Sept. Vol. 6. No. 3. pp. 439–445. With 3 figs. on 1 plate.

K. B. WILLIAMSON (1935) in a paper entitled " The Control of Malaria by Natural Methods," published in the *Malayan Agri-Horticultural Association Journal*, reprinted by the Eastern Bureau of the Health Organisation of the League of Nations, described his method of " Herbage Cover " to control mosquito breeding (see also this *Bulletin*, 1935, Vol. 32, pp. 429–30). Shallow watercourses are covered with packed grass and herbage, or with leaves of trees, with a few twigs intermixed, so as to form a brushwood drain. The herbage is well trampled under foot until it forms an almost solid wall which, according to Williamson, is impenetrable to egg-laying mosquitoes. In stagnant or slowly moving water sufficiently concentrated rotting, to prevent the breeding of malaria-carrying species, takes place.

Senior White, in this preliminary note, describes three experimental applications of the method in the Jeypore Hills Agency Tracts, Orissa. In the first experiment anopheline breeding was entirely eliminated, in a nullah so treated, from mid-October to the end of April. Similar success attended the second experiment. In the third no rotting took place, the packing merely acting as a rough sub-soil drain. As a consequence anopheline breeding was not eliminated. Culicine breeding was noted in all the experiments. It would appear that

ovipositing mosquitoes in large numbers can penetrate the packing, which " appears to act far less as a form of subsoil drainage than as a strictly biological control." This is in conflict with Williamson's findings : differences in the nature of the vegetation used may well account for the divergent results. It is evident from Senior White's experiments that much depends on the choice of scrub or vegetation used for packing. He considers that, for a thorough investigation into the method, the co-operation of both physiological and systematic botanists will be required.

As a method of mosquito control the method is very inexpensive. In it the author sees a definite hope for antilarval measures for the village. Not only may ravine and irrigation-channel breeding of anophelines be eliminated but the effluent from the " herbage covered " watercourse may well prove to have value as a rich liquid manure. The results of further experimental work along these lines will be awaited with interest. *N. W.*

Williamson (K. B.) & Scharff (J. W.). **Anti-Larval Sluicing.**— *Malayan Med. Jl.* 1936. Sept. Vol. 11. No. 3. pp. 123–150. With 2 diagrams & 11 plates. [24 refs.]

This paper contains a general account of sluicing as an anti-larval measure, based, for the most part, on careful experimental work carried out in Malaya for a number of years. The authors evidently consider that the lack of comprehension of fundamental principles has been responsible for certain unfavourable reports on the results achieved. Otherwise a more extended trial might have been made of a form of mosquito control that is inexpensive, easy to operate and adaptable to many conditions.

The difference between sluicing a channel and allowing it to empty itself into one already sluiced is insisted on. There is no evidence that larvae are carried down-stream alive as the result of sluicing ; the majority are either killed outright or are thrown up by the sluice wave on the banks to perish there. The characters of a sluice wave are described and illustrated.

Fear of erosion should not be a deterrent to the application of sluicing. Irregularly eroded channels may be unsuitable for sluicing but the erosive action of sluicing is little, if any, in excess of that of the normal flow and certainly less than that of natural spates. This of course does not apply to a small space immediately below the sluice gates, which may require special treatment. Sluicing is therefore applicable even to flat earth channels. The impounding of headwaters may present problems in connexion with mosquito breeding. The planting of shade plants, or the use of larvicides or other measures above the sluice, may be called for in certain cases. Automatic sluices have obvious advantages over the hand-operated varieties.

Numerous examples are given of the successful application of sluicing as an anti-larval measure in the Cameroon Highlands, Malaya, and in Penang. These descriptions are well illustrated with photographs. Some of the sluices described are of the simplest possible kind, their construction being within the competence of any handyman. One cannot but endorse the authors' plea for further trial in various conditions, for which they have made out a good case. *N. W.*

Casini (Guido). Sul cosi detto fenomeno dell'eliminazione dei globuli polari nei gametociti dei parassiti malarigeni. [**On the So-called Phenomenon of Elimination of Polar Globules in the Gametocytes of Malarial Parasites.**]—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. No. 2. pp. 88–98. With 6 figs. & 2 coloured plates. French summary.

Observations on malarial parasites of man and halteridium of birds have convinced the author that the so-called maturation of the female gametocyte by the extrusion of polar bodies is a misinterpretation of the events. What actually happens is a division of the nucleus, a true nuclear reduction, the no longer required chromatin being thrown out from the female gametocyte and being left in the residual body in the case of the male. Till this reduction has taken place fertilization is impossible. The process is compared with the well known phenomenon of the maturation of the ovum, and is illustrated by two coloured plates of the changes which take place in the malarial parasites. *C. M. Wenyon.*

Moschkovski (Sch.). Ueber einen eigentümlichen Fund in den von *Plasmodium vivax* befallenen Erythrozyten. [**Peculiar Occurrence in Red Cells infected with** *P. vivax*.]—*Rev. Microbiol., Epidémiol. et Parasit.* 1936. Vol. 15. No. 1. [In Russian pp. 57–59. With 21 figs. on 2 plates. German summary p. 59.]

In stained films of defibrinated blood of two patients with *Plasmodium vivax* infection there occurred commonly in the infected red cells, either in or outside the parasites, a deeply staining chromatin granule. It is assumed that it represents the caryosome of the parasite nucleus and that it had been displaced mechanically by the treatment to which the blood had been subjected. *C. M. W.*

Boyd (Mark F.). **On the Schizogonous Cycle of** *Plasmodium vivax*, **Grassi and Feletti.**—*Amer. Jl. Trop. Med.* 1935. Nov. Vol. 15. No. 6. pp. 605–629. With 1 text fig. & 124 figs. on 7 plates.

Corradetti (Augusto). Osservazioni sul ciclo schizogonico del *Plasmodium vivax*. [**On the Schizogonous Cycle of** *P. vivax*.]—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. No. 1. pp. 14–22. With 1 text fig. & 9 figs. on 1 plate. English summary.

A study of the morphology of a pure strain of *Plasmodium vivax* has convinced the author that five types of merozoite occur and that each of these, after entering red blood corpuscles, grows to its full size in a characteristic manner as judged by the structure of the nucleus. Merozoites of type A grow into schizonts which give rise to merozoites of type A, B or D. Those of types B and D grow into schizonts which give rise to merozoites of types C and E, which grow not into schizonts but into micro- and macrogametocytes respectively. There are thus five lines of growth, the individuals of each line being recognized chiefly by their nuclei but also to some extent by the character of the cytoplasm. The nuclei differ in size, shape and degree of development of the karyosome. The differences referred to are illustrated in a series of diagrams and microphotographs.

In the second paper the author states that he has failed to confirm the above observations and cannot distinguish the series A, B and D,

though he has noted that two kinds of mature schizont occur which differ as regards arrangement of pigment and merozoites. Furthermore the merozoites themselves differ in nuclear and cytoplasmic structure. The two types of rosette were noted by Golgi in 1889.

C. M. W.

Trensz (F.). La valeur pratique de la mélanofloculation de Henry. [**The Practical Value of Henry's Reaction.**]—*Arch. Inst. Pasteur d'Algérie.* 1936. Sept. Vol. 14. No. 3. pp. 353–390. [89 refs.]

The author describes at some length the conclusions at which he has arrived as the result of a very large experience of Henry's Reaction, to the literature of which he has contributed much. He insists on the necessity of a standardized technique : it is a delicate reaction. Variations in technique make it difficult to compare the results obtained by different authors. Samples of blood should be taken during periods of apyrexia and when the patient is fasting ; the serum should not be haemolysed. The author advocates the use of solutions of melanin, which he introduced, and the reading of the results with a photometer. The value of serological curves is discussed (see this *Bulletin*, 1937, Vol. 34, p. 62). During an attack of malaria the determination of the reaction is of little importance compared with the search for parasites, but in a patient who has recently suffered from fever, in whose blood no parasites are found, negative results with Henry's Reaction are of value in excluding malaria as a cause of that fever. In treatment it is of considerable value ; serological curves register the result of treatment especially in patients exhibiting post-febrile pathological conditions of spleen or liver. The curve continues to fall as long as the drugs employed are exercising a favourable action. The height of the index gives some indication in chronic cases as to the time that will be necessary for a complete cure to be effected but no indication of the immediate gravity of the illness. *N. W.*

Pampana (E. J.). **A Critical Interpretation of Some Experiments on the Treatment of Malaria.**—*Malayan Med. Jl.* 1936. Sept. Vol. 11. No. 3. pp. 154–160.

This lecture, delivered at the International Malaria course at Singapore, calls attention to the difficulty so frequently experienced in drawing any conclusions from observations recorded in malaria literature. Such observations, from lack of adequate control, or from neglect of consideration of factors that may have an important bearing on the subject under study, do not, in many cases, warrant the conclusion their authors derive therefrom. The examples quoted by Dr. Pampana are confined to papers dealing with the therapeutics of malaria. The study of the treatment of malaria in the field is inevitably attended with very great difficulty, and the author of this lecture has rendered very valuable service in calling attention in an able manner to some of the many pitfalls that trap the unwary. The paper merits wide publicity. If all workers in this important field had had clearer ideas of the complexity of the subject, contributions to the literature of the therapeutics of malaria would have been far fewer in number, but our knowledge of the subject might have been greater than it is to-day. *N. W.*

VAN SLYPE (W.). Atébrine injectable et paludisme aigu. [**Atebrin Injections and Acute Malaria.**]—*Ann. Soc. Belge de Méd. Trop.* 1936. Sept. 30. Vol. 16. No. 3. pp. 429–440. With 2 charts.

Eleven patients suffering from acute malaria were treated with intramuscular injections of dichlorhydrate of atebrin, thirty-three with intramuscular injections of atebrin musonate (dimethane-sulphonate). The doses used were those recommended by the makers. Both preparations were very efficient as antipyretics. Their action on schizonts was slower than it was on the temperature curve; the dichlorhydrate caused the total disappearance of parasites in 5 days, the musonate caused the disappearance in 91 per cent. of the patients in 11 days. Great prudence is necessary in the treatment of small children who are weakly; the authors think the doses recommended for small children are too large. Convulsions followed the injection in three children, one of whom died. Atebrin musonate, 0·125 gm. in 1 cc. of water, is tolerated just as well as when dissolved in 3 cc., the usual dilution. *N. W.*

EFENDIEV (M.), ADJALOV (S.), VINNITSKI (B.), GLASHKINA (T.), MELIKOVA (T.), RAKHMANOVA (E.), SADYKHOV (A.) & TARIVERDIEV (G.). [**Treatment of Malaria with Plasmocide and Acriquine.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1936. Vol. 5. No. 3. [In Russian pp. 422–425.]

An account is given of the results and methods of treatment of malaria with plasmocide and acriquine [the Russian equivalents of Fourneau 710 and atebrin respectively]. The observations on plasmocide are based on over 32,000 cases of all the three varieties, but mainly of M.T. The authors note the success of treatment in B.T. and Q., and the failure in M.T. cases In view of the toxicity of the preparation the daily dose is now reduced from 0·15 to 0·06 gm.

Acriquine was used in 900 cases (291 M.T., 48 B.T., 6 Q and 33 mixed infections) in doses of 0·1 gm. administered thrice daily *per os* for 7 days, followed by an interval of 3 days and a course of plasmocide for 5 days afterwards. The results of treatment are the same as in the case of atebrin, the only after-effect noted being the yellow colouration of the skin. *C. A. Hoare.*

AKASHI (Kazuyoshi), NAKASHIMA (Yoshio) & YŌ (Kinsei). Ueber Malariabehandlung mit Atebrin pro injectione (Atebrin Musonate).—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa).* 1936. Nov. Vol. 35. No. 11 (380). [In Japanese pp. 2463–2472. With 12 charts. German summary p. 2473.]

ROSA (A.), VALLI (E. Suzzi) & MACCOLINI (R.). Ancora sull'atebrin e la plasmochina nella bonifica umana antimalarica. [**Atebrin and Plasmoquine in the Treatment and Prevention of Malaria.**]—*Riv. di Malariologia.* Sez. I. 1936. Vol. 15. No. 4. pp. 258–288. With 1 map. English summary.

In five malarious villages in the Basso Ferrarese an attempt was made to control malaria by the administration of atebrin and plasmoquine to all sufferers from malaria and to all who had suffered from the disease during the previous season; no other measures for the

control of the disease were employed. At the beginning of the experiment a five days' course of atebrin was followed by an interval of six days when a three days' course of plasmoquine was given. Later on atebrin and plasmoquine were given together, daily for three days, and then atebrin alone during the succeeding two or three days. The latter treatment appeared to give better results and intolerance symptoms, rare in both cases, were less frequent. In three villages, where the houses are less crowded together than in the other two, and where communications with adjacent malarious centres are restricted, the results were excellent. In one village malaria has almost disappeared. In the remaining two villages the reduction in the incidence of malaria was much less marked. *N. W.*

Rao (B. A.) & Cheluvarayan (C.). **Mass Treatment and Prophylaxis with Atebrin.**—*Records of the Malaria Survey of India.* 1936. Sept. Vol. 6. No. 3. pp. 447–452.

The experiment described was carried out in the Bobbur Experimental Farm, Mysore, which has a stable population of 303. In April and again in November 1935 the majority of the population was submitted to a five days' course of atebrin, 0·1 gm. three times a day for adults. A month after the second course the same population was given a five days' course of treatment with plasmoquine, the adult dose being 0·01 gm. twice a day. In addition, from the 1st of January to the end of November 1935, each person received 0·02 gm. atebrin in a single dose on one day each week. One hundred and seventy persons completed the entire course. The spleen and parasite rates of these persons were 41·5 and 17·6 per cent. respectively in April 1935; in the following November these rates had been reduced to 10·7 and 0·6 per cent. There was no corresponding diminution of spleen and parasite rates in the adjacent Bobbur village, which served as a control. The malaria transmission season in this part of India is from August to December. The cost of such mass treatment is high, Rs.11 per head per year. *N. W.*

Fischer (Otto). Beobachtungen bei der Malariaprophylaxe mit Atebrin. [**Malarial Prophylaxis with Atebrin.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. Sept. Vol. 40. No. 9. pp. 397–400.

Two cases are described in which prophylactic administration of atebrin protected completely against malarial infection.

In the case of one patient the author advised him to take whilst in the highly malarial parts of the Cameroons alternately ½ and 1 tablet of atebrin daily, gradually reducing the dose to ½ tablet daily (each tablet contains 0·1 gm. atebrin). This scheme of prophylaxis was carried out during more than 2½ years with very good results and the person was able to continue his work without interruption. He had no unpleasant toxic symptoms. The skin had a sunburnt appearance. It was found that the smaller dose was efficient as a prophylactic. The other case was a female, aged 27, who was in East Africa from 1931 to 1936. From 1935 she was given prophylactically 3 atebrin tablets weekly, because quinine was causing palpitation and insomnia. The atebrin caused no unpleasant symptoms, the skin showed the same sunburnt appearance. She remained free from malarial infection. He warns against the simultaneous administration of atebrin and plasmoquine as likely to produce toxic symptoms. *E. D. W. Greig.*

Bispham (W. N.). **A Report on the Use of Atabrine in the Prophylaxis of Malaria.**—*Amer. Jl. Trop. Med.* 1936. Sept. Vol. 16. No. 5. pp. 547–562.

In many areas in the Southern states, in which Civilian Conservation Corps Camps were established in 1933, malaria has been an important cause of morbidity among the enrollees. It was not possible in many cases to eliminate malaria by general antimalaria measures. In 1934 all the inhabitants of the camps had their blood examined once a month ; whenever parasites were found the carrier was treated with atebrin, 4½ grains a day for five days. Thereafter the blood of each carrier was examined every two weeks till the end of the year. Nearly all cases were *P. vivax* infections. In 1935 this measure was supplemented ; whenever a camp had five malaria cases in a week the entire personnel were given three grains of atebrin a week until the number of cases had fallen to a negligible point. The average strength of a camp approximated two hundred.

The authors conclude that, as a prophylactic, atebrin is far superior to quinine ; increased doses would probably give still better results. In the treatment of *vivax* infections atebrin is superior to quinine ; it is also cheaper as much smaller amounts are required. *N. W.*

Winchester (M. E.). **Individual Chemoprophylaxis against Malaria. Preliminary Report.**—*Southern Med. Jl.* 1936. Oct. Vol. 29. No. 10. p. 1029.

An interesting experiment to determine the value of atebrin as a prophylactic. In a highly malarious part of Georgia two groups, each consisting of 28 families, living in exactly similar conditions, were selected. In the prophylactic group the spleen rate was 46 per cent., the parasite rate 7·8 per cent. In the control group the spleen rate was 32 per cent., the parasite rate 10·4 per cent. In April 1935 all persons with positive blood smears, in both groups, were given a complete course of atebrin. On May 15th prophylaxis was started : each individual in one group took a 50 mgm. tablet of atebrin with the evening meal. The members of the control group were left to their normal self-medication. This was continued till the 1st of November. During the spring and summer there were 58 cases of malaria in the control group, none in the prophylactic group. The type of malaria is not stated. *N. W.*

Berny (P.) & Nicolas (L.). Note sur la campagne antipaludique effectuée en 1936 à la crique anguille (Guyane française) avec la médication mixte (quinacrine-rhodoquine). [**Prophylaxis of Malaria with Quinacrine and Rhodoquine in French Guiana.**]—*Bull. Soc. Path. Exot.* 1936. Oct. 14. Vol. 29. No. 8. pp. 870–872.

A description of a successful attempt to control malaria in a penitentiary, 39 kilometres from Cayenne, French Guiana. The population affected varied between 101 and 138 ; it was, for the most part, a stable population and all adults. Malaria infections were almost exclusively *falciparum*. The vector was *A. albitarsis*.

In November 1935 the parasite index was 13 ; at the end of the following month it was 21. Drug prophylaxis began on the 1st of January 1936. Each Sunday each man was given quinacrine 0·30 gm. and rhodoquine 0·02 gm. This was continued for six months. There

was no sign of drug intolerance and no interference with work. Early in April the parasite index had fallen to 1 and the general health conditions of the group were excellent. At the end of the treatment the parasite index was zero. In the neighbourhood malaria was very prevalent.

[In the discussion of this paper Ph. Decourt pointed out that experience elsewhere had shown that it was sufficient to administer this mass " mixed prophylaxis " twice a month.] *N. W.*

Manwell (Reginald D.) & Herman (Carlton). **The Occurrence of the Avian Malarias in Nature.**—*Amer. Jl. Trop. Med.* 1935. Nov. Vol. 15. No. 6. pp. 661–673. [14 refs.]

The examination of 652 birds, the majority of which were caught in the neighbourhood of Syracuse (New York), for evidence of malarial infection has shown that 54 were infected with representatives of seven known and one unknown species of *Plasmodium*. The procedure of inoculating blood into English sparrows or canaries, practised in 127 cases, gave much better results than other methods used for detecting parasites. *C. M. W.*

Wolfson (Fruma). **Bird Malaria transmitted by the Intravenous Injection of Sporozoites.**—*Jl. Parasitology*. 1936. June. Vol. 22. No. 3. pp. 291–292.

In two out of three experiments canaries were infected with bird malaria by the intravenous injection of sporozoites from *Culex pipiens*. Previous attempts by other observers have failed, though it is well known that human beings can be infected by intravenous injection of sporozoites from Anopheles. In the case of the two infected birds parasites were first seen about the tenth day. *C. M. W.*

Raffaele (Giulio). Potere infettante del sangue durante l'incubazione della malaria aviaria. [**Infectivity of Blood during the Incubation of Avian Malaria.**]—*Riv. di Malariologia*. Sez. I. 1936. Vol. 15. No. 2. pp. 77–87. English summary.

It is well known that after malaria-infected mosquitoes are allowed to feed on a susceptible host parasites do not appear in the blood for some days. The assumption is that the sporozoites do not directly enter the red blood corpuscles but that some form of development occurs outside the blood stream during the latent period and that finally there are produced the red-cell-invading forms. The author has still further tested the absence of parasites from the blood by injecting into fresh canaries blood taken from canaries at varying intervals after mosquitoes infected with *Plasmodium relictum* had fed on them. In this way it was shown that parasites do not appear in the blood before the sixty-fifth hour. The infections produced by blood taken on the third or fourth day are characterized by their mildness. *C. M. W.*

Sinton (J. A.). **Studies in Immunity in Malaria. Part V. The Nature of the Tolerance shown by *Silenus irus* to Infection with *Plasmodium knowlesi*.**—*Records of the Malaria Survey of India*. 1935. Dec. Vol. 5. No. 4. pp. 501–521. [20 refs.]

It is well known that the monkey *Silenus irus* (*Macacus cynomolgus*), as it is procured in India, is very tolerant of experimental infection

with *Plasmodium knowlesi*. In this respect it differs from the highly susceptible *Silenus rhesus* (*Macacus rhesus, Macaca mulatta*). All attempts to break down this resistance by varying the dosage of parasite and virulence of strains used failed entirely, so that the author was led to the conclusion that the tolerance is something inherent in this species of monkey, though it has not been possible to test laboratory-bred monkeys, which would be known to have had no previous infection. Splenectomy, however, is capable of bringing about a severe relapse of a latent infection and if performed before inoculation will render the animal highly susceptible. The general conclusion is that the tolerance is bound up with tissues, probably reticulo-endothelial cells, of the spleen, and not with immune substances in the blood serum, unless it be assumed that splenectomy causes rapid disappearance of these. *C. M. W.*

Nauck (E. G.) & Malamos (B.). Thorotrast-Speicherung bei experimenteller Affenmalaria (*Pl. knowlesi*). [**Thorotrast Blocking in Experimental Monkey Malaria** (*Pl. knowlesi*).]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1936. May. Vol. 40. No. 5. pp. 187–197. With 7 figs. [21 refs.]

The authors have found that intravenous and intraperitoneal injections of colloidal Thorium Dioxid-Sol (Thorotrast) have no influence on the course of *Plasmodium knowlesi* infection in monkeys, though the material is taken up by the reticulo-endothelial cells, as evidenced by X-ray photography and post-mortem histological examination. There thus appears to be no functional blocking of the reticulo-endothelial system by thorotrast. *C. M. W.*

Shute (P. G.) **A Simple Method of rearing and maintaining** *Anopheles maculipennis* **throughout the Year in the Laboratory.**—*Jl. Trop. Med. & Hyg.* 1936. Oct. 15. Vol. 39. No. 20. pp. 233–235. With 3 figs.

The author describes methods which have been used successfully for several years to maintain a supply of *Anopheles maculipennis* (no doubt of the race *atroparvus*) in the laboratory.

The early stages are reared in shallow earthenware pans about 18 in. (50 cm.) in diameter. Strips of grass and grass roots are cut and stuck round the edge of the pan close to the water level, and it is found that as many as 300 larvae will grow up successfully in such a pan, and that they do not require artificial food. It has been noticed that in spite of artificial heating some females tend to hibernate in the autumn and winter, and that it is much more difficult to obtain a supply of eggs at that season than in summer.

A special insectary has been built heated electrically and with thermostatic control of temperature, and a small pig kept in it as food for the insects. In the stock which has been maintained continuously for three years the author has observed a considerable range of variation in the colour of the eggs and in the number of ridges in the floats, but in spite of the variation none of the batches of eggs could have been attributed to any race other than that to which they belonged.

P. A. Buxton.

DE JESUS (P. I.). **Physicochemical Factors in Anopheline Ecology, I : Studies on Nitrogen.**—*Philippine Jl. Sci.* 1936. Apr. Vol. 59. No. 4. pp. 473–491. [24 refs.]

The contents of the paper are indicated by its title. The author demonstrates in a quantitative manner that *Anopheles minimus* var. *flavirostris* breeds in clean, unpolluted water, of which the nitrogen content is low.

After giving a partial review of the literature on a subject which has attracted much attention, the author turns to a study of those nitrogenous substances in water which may be presumed to influence the species under study. He has collected 170 samples of water, making a count of larvae at the same time. The first table sets out the frequency of larvae of *minimus* and other species at different concentrations of ammonia nitrogen. It is clear that the larvae of *minimus* were most frequently found when the concentrate was under 0·1 part per million. But the larvae may occur when the concentration is as high as 0·35 : beyond that figure there are no records, but it is not clear from the table whether any water samples were examined in which the ammonia passed that figure, larvae not being found. Other tables deal in a similar way with the distribution of larvae, with reference to concentration of other nitrogenous materials. *P. A. B.*

SIMATCHKOVA (M. S.). **The Factors influencing the Distribution of the Mosquitoes *A. maculipennis* in the Diurnal Resting Places.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1936. Vol. 5. No. 4. [In Russian pp. 549–564. With 7 figs. [11 refs.] English summary p. 565.]

In the interior of buildings the resting places of *A. maculipennis* are determined by various factors making up the microclimatic conditions. Where there is no draught and no direct sunlight, temperature and humidity are the prevailing factors. The author found that with a relative humidity below 65, the number of mosquitoes and the degree of humidity ran parallel ; this did not hold good with a higher degree of relative humidity. Determining factors then were light and draughts. If the humidity is adequate and there is no draught and no bright illumination the distribution is fairly equal. Where temperature is low, they preferred the higher levels near the ceiling ; with higher temperature, they settle nearer the floor, but only if the temperature beneath their level is lower. It is concluded that at the usual summer temperatures the optimal zone of humidity is at 65 per cent. Migration within a building was found to depend on the length of time after feeding, *i.e.*, on the stage of blood digestion. *H. H. S.*

THOMPSON (T. O.). **Mosquito Destruction by James' Method.**—*Jl. Roy. Army Med. Corps.* 1936. Nov. Vol. 67. No. 5. pp. 331–335. With 5 figs.

J. F. James's method of fumigation and trapping mosquitoes was referred to in this *Bulletin* (1935, Vol. 32, p. 818). It is now used as a routine anti-malaria measure in the barracks in Bannu, India, and the results obtained are described in this paper. "The stream of mosquitoes which pour out of a room to the lighted opening to escape from this

fumigant has to be seen to be believed." Annual catches of mosquitoes have been from 15,000 to 18,000, of which the majority have been anophelines. *N. W.*

OMAR (Wasfy). **A New Larvicide.**—*Jl. Egyptian Med. Assoc.* 1936. Oct. Vol. 19. No. 10. pp. 592–608.

Acid-oil-sludge is a waste product of the operation of refining the benzine and kerosene distillates of crude oil. It is a very thick reddish-black acid liquid of no commercial value. If one part of this sludge be added to 1,000 parts of water containing larvae and pupae of anophelines or culicines all such developmental forms die within a few hours. The larvicidal action of the sludge is attributed chiefly to its soluble ingredients. *N. W.*

BLACKWATER FEVER.

Dimissas (C. A.). Quelques observations sur l'épidémiologie de la fièvre bilieuse hémoglobinurique en Grèce. [**Some Observations on the Epidemiology of Blackwater Fever in Greece.**]—Paper presented at Panhellenic Med. Congress, Thessalonica, 1935. [Original in Greek 34 pp. With 8 figs. [38 refs.] Summary prepared from a French résumé supplied by author.]

The author records a number of observations on the incidence of blackwater cases in malarial districts of Greece, and from these observations he draws certain conclusions.

He found that in the same region, in towns and villages having the same amount of malaria, the inhabitants of which were living under the same conditions and belonged to the same race, blackwater fever occurred in certain places and not in others. His attention was first drawn to this fact in 1920 when he had to deal with a small epidemic of the disease at Comotini; between September and November of this year he encountered 60 cases in a certain quarter of the town. No case was seen in any of the surrounding villages, although malaria was particularly intense. In 1928, he made similar observations at Paros, information concerning which is given in some detail. Reference is also made to similar observations made by other writers in Greece and elsewhere.

The number of cases and even the severity of the disease varies in different years. Most of the cases occur during the autumn, and the disease is more common among children and adolescents than among adults. Instances of the disease were often found in the same house in people unrelated to one another. A decrease in the number of cases of blackwater fever in a district appears to follow a diminution in the amount of malaria and in the number of anophelines.

From these observations the author draws a number of conclusions. He considers that blackwater fever presents itself as a nosological entity which is specially and intimately connected with malaria. The cause of the disease is probably a haemolytic strain or variety of *Plasmodium falciparum*. Individuals who react well to small infections of blackwater fever acquire an immunity (premunition); those who do not react well or in whom the premunition is exhausted or diminished by external causes such as cold, fatigue, quinine, etc., develop typical blackwater fever. *W. Yorke.*

Hernández Gómez (J. G.). Nuevas consideraciones sobre el sindrome febril icterohemoglobinurico. [**Fresh Considerations on the Blackwater Fever Syndrome.**]—*Gac. Méd. de Caracas.* 1935. July 15. Vol. 42. No. 13. pp. 193–194.

After some preliminary remarks the author states "although the malaria plasmodium is not the [sole] cause of the bilious haemoglobinuric syndrome we believe that there is no syndrome in the absence of the plasmodium" and later "when during the haemoglobinuric period a strong dose of quinine is given without any preceding administration of antihaemolytics, there is nearly always a violent access of fever with haemoglobinuria, which may or may not cease when the drug is stopped," but if antihaemolytics have been given, though there may be similar accessions of fever, haemoglobinuria will

not occur. If atebrin is given in the pre-haemoglobinuric stage, in place of quinine, the febrile attacks lessen in severity and haemoglobinuria does not occur. If the atebrin is given in the haemoglobinuric stage the symptoms begin to clear up and if antihaemolytics be given as well, the results are surprisingly good. The ideal treatment he affirms is " Prevent haemolysis, restore to the red corpuscle its normal resistance by use of antihaemolytic substances and at the same time attack the parasite without jeopardizing the life of the patient." [Sound in theory but unfortunately the author does not tell us what " antihaemolytic " he utilizes for this purpose.] *H. H. S.*

WITTS (L. J.). **The Paroxysmal Haemoglobinurias**—*Lancet.* 1936. July 18. pp. 115–120. With 3 figs. [26 refs.]

This paper is an interesting review of the various paroxysmal haemoglobinurias. Haemoglobin is present in the body in two distinct forms, the haemoglobin of the red cells and the myohaemoglobin of the muscles. Myohaemoglobinuria is more familiar to veterinarians than to physicians and is not uncommon in horses and probably other domestic animals.

True haemoglobinuria is usually, if not always, the result of intravascular lysis of the red corpuscles, and in cold haemoglobinuria and in blackwater fever it has been clearly demonstrated that haemoglobinaemia always precedes the haemoglobinuria. A description of each of the following types of haemoglobinuria is given and the descriptions are illustrated by references to cases : " Haemoglobinuria e frigore " ; " Haemoglobinuria from exertion " ; " Haemoglobinuria recurrens vel nocturna cum anaemia haemolytica (Marchiafava-Micheli) " ; " Paroxysmal Haemoglobinuria with Stengel's splenomegaly."

In his conclusions the author writes as follows :—

" It is only by ranging the different varieties of haemoglobinuria alongside each other that we can separate the symptoms which are common to all forms of haemoglobinuria from those which are peculiar to the individual examples, nor can it be without value to be familiar with the forms of haemoglobinuria whose mechanism has been elucidated before trying to solve such a difficult riddle as the nature of blackwater fever.

" (*a*) Haemoglobinuria is usually if not always the result of intravascular haemolysis and haemoglobinaemia.

" (*b*) Symptoms common to all forms of haemoglobinaemia and haemoglobinuria are shock, anaemia, diminution or suppression of urine, and thromboses in various parts of the vascular tree.

" (*c*) Recurrent or paroxysmal haemoglobinuria is not always syphilitic, and the following types can be distinguished :—

" 1. Haemoglobinuria e frigore, in which the blood is lysed by exposure to cold either in vivo or in vitro, and which is usually if not always due to syphilis.

" 2. Haemoglobinuria from exertion, which is a relatively harmless abnormality occurring in young males. It is probably similar in pathology to postural albuminuria and spontaneously disappears in adult life.

" 3. Haemoglobinuria, usually nocturnal, associated with haemolytic anaemia. This is an intractable disorder of unknown aetiology with a bad prognosis.

" 4. Paralytic haemoglobinuria, in which the pigment is derived from the muscles and the attacks of myohaemoglobinuria are associated with weakness and paralysis of the skeletal muscles.

"I have arranged the different types in order of frequency. There is reason to believe that other forms of paroxysmal haemoglobinuria also occur, but such forms as do not belong to one or other of the above four groups must be excessively rare." *W.Y.*

HAMBURGER (Louis P.) & BERNSTEIN (Alan). **Chronic Hemolytic Anemia with Paroxysmal Nocturnal Hemoglobinuria**—*Amer. Jl. Med. Sci.* 1936. Sept. Vol. 192. No. 3. pp. 301–316. [40 refs.]

After a brief review of the various haemoglobinurias the authors describe two cases of an uncommon type of chronic haemolytic anaemia associated with paroxysmal haemoglobinuria.

The haemoglobinurias may be of exogenous origin and associated with infections and intoxications; recently a new member was added to this group when the discovery was made that the consumption of fish or eels containing resinous acids was followed by a malady, a feature of which is haemoglobinuria. This disorder is indigenous in the vicinity of Königsberg and is known as Haffkrankheit (STOELTZNER 1932) [See *Bull. of Hyg.* 1933, v. 8, 505, 506, 632; 1934, v. 9, 55, 411, 412.] Another condition associated with haemoglobinuria is "favism," which is caused by the inhalation from blossoming bean plants of the species *Vicia fave* or by the ingestion of the beans.

Haemoglobinurias of endogenous origin are cold haemoglobinuria, march haemoglobinuria, and the so-called paralytic haemoglobinuria. A fourth type was added in 1931, when MICHELI described a well-defined clinical entity, a prominent feature of which was paroxysmal haemoglobinuria. Two new instances of this uncommon type of haemoglobinuria are the subject of the present paper.

The patients suffered from chronic anaemia associated with paroxysmal haemoglobinuria. The urinary discolouration occurred chiefly at night. Concomitant variable symptoms and signs of the syndrome are abdominal, lumbar and substernal pain, jaundice and fever. The chief blood changes are an anaemia which may become profound, reticulocytosis, and perpetual haemoglobinaemia. The urine always contains a little urobilin and haemosiderin. The patient may live for years and therapeutic measures are of little avail. Splenectomy is dangerous and without benefit; and the same applies to blood transfusions.

The authors discuss the differential diagnosis of this condition from other paroxysmal haemoglobinurias, haemolytic anaemias, and congenital haemolytic icterus. *W. Y.*

FERNÁN-NÚÑEZ (M.) **Hemoglobinuric Fever: is it an Allergic Phenomenon?**—*Amer. Jl. Trop. Med.* 1936. Sept. Vol. 16. No. 5. pp. 563–577. [23 refs.]

This paper reviews the various theories of the aetiology of blackwater fever advanced by numerous investigators, and submits evidence to support the author's thesis that the disease is essentially of allergic origin. Observations were made on about 100 cases encountered by the author during 5 years' practice in the Magdalena river valley of Colombia.

After briefly reviewing "the specific theory," the "malaria theory" and the "quinine theory" which have been advanced to explain the

condition of blackwater fever, the author passes to a consideration of his " allergy theory." He writes as follows :—

" The story of blackwater fever then seems to be : A non-immune person has an attack of subtertian malaria during his first two years of residence in a malarial district. This may produce an immunity, but if the immunologic process goes wrong he may be sensitized to the disease instead in the way the first attack of tuberculosis sensitizes the patient (childhood type of tuberculosis). A subsequent attack of estivo-autumnal malaria (after approximately two years of residency there) produces an allergic reaction with destruction of the sensitized erythrocytes, just as a subsequent attack of tuberculosis produces pulmonary tuberculosis with cellular destruction (adult type of tuberculosis). One attack predisposes to other attacks, 10 per cent. of all cases having recurrences, sometimes as many as ten different attacks (not relapses).

" Symptoms of blackwater fever usually appear promptly after infection by a mosquito bite (within 12 days), [This is a strange statement. What about the attacks of blackwater fever which occur in malarial patients after their return to England and other non-malarial countries ?] while the incubation periods of first attacks of malaria may be as much as six months, depending upon the resistance of the host. Fortunately the risk of death is largely confined to the first attack as tolerance is quickly acquired, probably by saturation of the allergic receptors attached to the cells, as is seen in the gradual desensitization in hay-fever by repeated pollen injections. Whether immunity or allergy will occur in a given individual seems to depend upon the state of the general health. In persons with lowered resistance allergy seems more prone to occur, paroxysms of haemoglobinuria usually following malnutrition, chronic organic disease, an intercurrent infection, debility or alcoholism, excessive fatigue and being ushered in by a chilling of the body, excitement or depression, which may cause great activity in the spleen, it even contracting to one quarter its normal size.

" This allergy could result from sensitization by protein antigens of the malaria parasites, the allergic attacks being precipitated by a reinfestation or reactivation of a latent infection of the same species or strain of plasmodium. Quinine by destroying the parasites could liberate the allergens quickly and bring on an attack, thus accounting for the fear of the use of quinine in blackwater fever. It is well known that a slight dose of quinine can precipitate a fatal attack of hemolysis and that there is no relationship between the number of parasites and the severity of the paroxysms.

" The numerous cases of blackwater precipitated by treatment of malaria with Atebrin and Plasmochin reported by Banerjee, Moir and others suggest a rôle similar to that played by quinine.

" The blood is often negative for malaria parasites during or after an attack of hemoglobinuric fever, which fact strongly suggests their universal destruction by a hemoclastic process. This destruction of the parasites often cures the disease spontaneously, *i.e.*, without quinine. This frequent absence of parasites was greatly confusing to the earlier investigators and led them to search for a cause other than malaria.

" Of course, it is possible that the hemoglobinuria in some instances is due entirely to quinine allergy. Blackwater is certainly much more common in persons with quinine idiosyncrasy. It is probable, however, that the attacks of quinine hypersensitiveness serve only to precipitate the anaphylactic picture, just as does chilling of the body, exhaustion, etc. Death has occurred within twenty-four hours after taking quinine, quite evidently due to anaphylactic shock."

The author describes what he considers to be a method of prophylaxis. A suspension of parasitized red cells containing *P. falciparum* was made by the method of Bass. To this 0·4 per cent. of formalin was

added as a preservative. Persons of white or mixed ancestry who had lived in the Lebrija river valley of Colombia for 6 months or more—a region where blackwater was very common—and who gave a history of malignant tertian malaria, were injected intracutaneously with 0·2 cc. of the suspension. Of 410 individuals so tested 16 showed a positive reaction characterized by local inflammation, appearing within 12 hours, and followed by a reddish discoloration (haemolytic?) which turned black within a few days, then brown, yellow and eventually faded away in less than 2 weeks. "All persons showing a positive reaction were invalided to a non-malarious climate, and blackwater fever disappeared from the community." Thus, writes the author, the control of aestivo-autumnal malaria, or the removal of those showing allergy to it, would appear to eliminate blackwater fever from any region. *W. Y.*

Armentano (L.) & Bentsáth (A.). Hämoglobinurie und Vitamin C. [**Haemoglobinuria and Vitamin C.**]—*Klin. Woch.* 1936. Oct. 31. Vol. 15. No. 44. pp. 1594–1596. [15 refs.]

A patient suffering from paroxysmal haemoglobinuria was found to be highly deficient in ascorbic acid, and it was decided to ascertain whether the administration of this substance had any action on the disease. Details of the case are as follows.—The patient, aged 36, came under observation on 10th December, 1935. He gave a history of attacks of paroxysmal haemoglobinuria for 2 years. The man was pale, the erythrocyte count was 2,500,000, haemoglobin 42 per cent., leucocytes 8,100, and thrombocytes 270,000; spleen not palpable; syphilis in youth, Wassermann reaction ++++. On 13th December a cold foot-bath produced an attack of paroxysmal haemoglobinuria. On 18th December the Donath-Landsteiner reaction was positive, and another cold foot-bath produced a typical attack. On 28th December Vitamin C, 600 mgm., was given intravenously and 5 minutes later exposure to cold failed to produce an attack of haemoglobinuria, although the Donath-Landsteiner reaction remained positive. On 14th January 1936, exposure to cold produced a typical paroxysm of haemoglobinuria. From 16th to 31st January the patient was given daily an intravenous injection of 300 mgm. of Vitamin C. On 1st February and on subsequent dates up to 31st May numerous attempts to produce an attack of haemoglobinuria by exposure to cold failed.

The authors believed that ascorbic acid acts by decreasing the amount of autohaemolysin; they note that saturation of the patient with Vitamin C caused the Wassermann reaction to become negative. It is considered that this work justifies a trial of ascorbic acid in blackwater fever. *W. Y.*

Dickson (J. G.). **Paroxysmal Hemoglobinuria. With Report of a Case followed for 13 Years.**—*U.S. Nav. Med. Bull.* 1936. July. Vol. 34. No. 3. pp. 300–306. [16 refs.]

A general account of the disease with special reference to a case which came to the author's notice.

The patient—a man aged 40—first came under observation in January 1922, complaining of chills and bloody urination following exposure to cold. He dated his illness to the summer of 1918 when, on duty of mine-planting in the North Sea, he became abnormally susceptible to cold.

In March, 1922, he was admitted to the United States Naval Hospital. The Donath-Landsteiner test was positive. After the patient had been placed in the ice-box at 5°C. for 45 minutes, he developed a rigor when he came out and voided red urine. The Wassermann reaction was positive ; and the leucocyte count was 13,950. The spinal fluid was normal. The patient was given injections of mercury succinimide and neoarsphenamine, and discharged to duty after 3 of each with a recommendation that 5 more injections of neoarsphenamine be given before allowing a rest period.

The patient has not been seen since 1922, but on April 15th, 1935 he wrote that he is now in excellent health and has never had any more " bloody discharges," and has had no further treatment. *W. Y.*

GÜNTHER (Carl E. M.). **A Case of Blackwater Fever showing Intermittent Haemoglobinuria.**—*Med. Jl. Australia.* 1936. Apr. 18. 23rd Year. Vol. 1. No. 16. pp. 542–543. With 1 chart.

A clinical account of a case which presented no features of special interest. *W. Y.*

AKASHI (Kazuyoshi). Ueber den Kochsalzgehalt des Blutes beim Schwarzwasserfieber. [**On the Sodium Chloride Content of the Blood in Blackwater Fever.**]—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Mar. Vol. 35. No. 3 (372). [In Japanese pp. 602–622. With 8 charts. [11 refs.] German summary p. 623.]

The author estimated the sodium chloride content of the plasma, whole blood, and red cells in a series of 30 healthy men and the same number of healthy women, and he compared the results with his findings in 8 cases of blackwater fever.

In blackwater fever the sodium chloride content of the plasma decreased during the paroxysm, but during recovery it rose so as to exceed the normal, and then finally returned to the normal value.

In whole blood the sodium chloride content rose during the paroxysm on account of the considerable decrease in the volume of the red cells. After the attack it fell towards normal, then rose again, and finally returned to normal. These fluctuations shown by the whole blood are, of course, determined in large measure by the decrease and subsequent increase in the volume of the red cells. *W. Y.*

AKASHI (Kazuyoshi). **The Treatment of Blackwater Fever with Sodium Bicarbonate.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1936. Mar. Vol. 35. No. 3 (372). [In Japanese pp. 591–601. With 3 charts. [23 refs.]. English summary p. 601.]

Four cases of blackwater fever were treated by daily intravenous injections of 100 cc. to 300 cc. of a 5 per cent. solution of sodium bicarbonate ; this was combined with oral administration of 3 gm. to 7 gm. of sodium bicarbonate daily. Owing to vomiting, the author regards the oral administration as of little importance. Three of the 4 patients recovered ; in 2 of these the urine cleared quickly and in all 3 cases diuresis increased remarkably after the injections. *W. Y.*

MOREAU (P.). Quinacrine et fièvres bilieuses. [**Quinacrine and Blackwater Fever.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1936. Feb. Vol. 14. No. 2. pp. 228–249. [134 refs.]

A general discussion of the relative merits of quinine and atebrin in the treatment of malaria with special reference to the value of the latter in blackwater fever cases. It contains no new observations.

W. Y.

SAMPEDRO (Mariano Maldonado). Un caso de fiebre hemoglobinurica tratado con exito por la atebrina compuesta.—*Medicina Países Cálidos.* Madrid. 1936. June. Vol. 9. No. 6. pp. 269–283. With 1 chart. [54 refs.]

VAN WAARDENBURG (D. A.). Over een geval van zwartwaterkoorts behandeld met biocholine.—*Geneesk. Tijdschr. v. Nederl. Indië.* 1936. Apr. 21. Vol. 76. No. 16. pp. 1001–1004.

RABIES.

A REVIEW OF RECENT ARTICLES. XXVI.*

A number of papers have appeared in which the transmission of rabies by the vampire bat is discussed. The first of these by VERGE and GORET[1] is for veterinary consumption and deals mainly with the historical and geographical aspects of the problem. It appears that epizootics of paralytic rabies have been observed throughout a belt of country extending from Trinidad in the North, through the central parts of Brazil, and the Matto Grosso, and reaching the sea in the south on a front extending from San Paulo to Monte Video.

In the second TORRES and LIMA[2] report further experimental work carried out at Rio de Janeiro. This is a lengthy paper dealing with the examination of the virus obtained from bats, its properties, the symptoms of infection in the bat, the disease in cattle, and the existence of bats which are " carriers " of the disease.

The third, also by TORRES and LIMA,[3] deals with rabies in the bat, the course of the disease, the virulence of the saliva, the transmission of the disease from bat to bat, and the pathological changes found in the brain.

In the fourth by PACHECO and PROENÇA,[4] it is reported that the virus can be found in the blood of infected animals, and that the disease can be transmitted by injection into the veins.

In the section on Rabies in the *Boletín de la Oficina Sanitaria Panamericana*[5] the whole question of cattle epizootics in South America, and the transmission of the disease by the bat is summarized. In addition to this there are reviews of various papers relating to rabies in general, and in particular to the incidence of rabies in South America.

" Since the British occupation of Tanganyika Territory no case of human or dog rabies has been confirmed. In the German records 3 cases of dog rabies are reported, but so far a search of the records has failed to reveal a case of human rabies." During 1933 and 1934 several suspicious cases of rabies in animals occurred, and two human deaths were reported, but in no case was the diagnosis confirmed. In 1935 a European officer died of rabies in Edinburgh whilst on leave from Tanganyika Territory. A case is now reported from the Central

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* For the twenty-fifth of this series see 1936, Vol. 33, p. 742.

[1] VERGE (J.) & GORET (P.). Sur un nouveau mode de transmission de la rage. A propos des épizooties de rage paralytique transmise par la morsure des vampires.—*Rec. Méd. Vét. Exot.* 1936. Apr.–June. Vol. 9. No. 2. pp. 41–54. With 4 figs. [38 refs.]

[2] TORRES (Sylvio) & LIMA (E. Queiroz). La rage et sa transmission par les vampires.—*Rev. Gén. de Méd. Vét.* 1936. Aug. 15. Vol. 45. No. 536. pp. 449–478.

[3] TORRES (Sylvio) & LIMA (E. de Queiroz). A raiva nos morcegos hematophagos. (*Desmodus rotundus murinus.*)—*Rev. Depart. Nac. da Producção Animal.* Rio de Janeiro. 1935. Vol. 2. Nos. 4, 5 & 6. pp. 385–396. With 10 figs. English summary.

[4] PACHECO (Genesio) & PROENÇA (M. Cavalcanti). O virus da raiva bovina do Brasil circula no sangue e se pode transmittir por via sanguinea. (Nota previa.)—*Brasil-Medico.* 1936. Aug. 1. Vol. 50. No. 31. p. 661.

[5] BOLETÍN DE LA OFICINA SANITARIA PANAMERICANA. 1936. May. Vol. 15. No. 5. pp. 473–477.—Rabia.

Province by WILSON and SINGH.[6] The diagnosis was confirmed by the presence of Negri bodies.

The prevalence of rabies during 1935 in Cuba is discussed by ARENAS MARTORELL and HERRADA LLIBRE[7] (see also this *Bulletin*, 1936, Vol. 33, p. 324). Charts show that "the epidemic" reached a maximum during the month of February.

According to BAKER, MCALPINE and DOWLING,[8] rabies is becoming increasingly prevalent in the southern States of America. In Florida the number of dogs' brains examined and found to be positive during the years 1929–1934 was 4,256, and the average annual increase was computed to be 15·6 per cent. In Texas the number was 2,757 and the annual percentage increase 16·8. Similar though lesser rates of increase occurred in Tennessee, Georgia and Mississippi, whilst in Florida there was a decrease of 29·1 per cent. Various statistics are given regarding the number of treatments issued, the location of the bite, and the occurrence of paralytic accidents (2 amongst 20,517 persons treated).

i. *Virus.*

The experiments of NICOLAU and KOPCIOWSKA[9] on the reconversion of fixed virus into street virus have been frequently referred to in these reviews (1934, Vol. 31, p. 637 and 1935, Vol. 32, p. 605). In these earlier experiments it was difficult to obtain an unbroken line of subpassages, as from time to time the nerve trunks injected proved to be avirulent. They then inoculated, in addition to the portion of nerve trunk, an emulsion from the related spinal ganglion. By this procedure difficulties were reduced but still failures were encountered. If a small fragment of lumbar cord is also added the results of inoculation are constant, passages are carried out with certainty, and the numbers of Negri bodies in the oculomotor nuclei and in the spinal ganglia increase steadily in number with subpassage. The procedure which they now adopt is to inoculate a fraction of this mixture into the sciatic nerve trunk.

The properties of the strain of fixed virus in use at Beirut have been examined by P. and A. MILLISCHER.[10] The procedure adopted was that of REMLINGER and BAILLY, and the results are given in detail.

The characters of the Sassari virus are discussed by LÉPINE and SAUTTER.[11] As is well known, this strain of fixed virus is peculiar in that it is virulent when inoculated subcutaneously into laboratory

[6] WILSON (D. E.) & SINGH (Hari). A Case of Human Rabies in the Central Province of Tanganyika.—*East African Med. Jl.* 1936. Sept. Vol. 13. No. 6. pp. 185–186.

[7] ARENAS MARTORELL (Rogelio) & HERRADA LLIBRE (Manuel). Estado actual de la rabia en Cuba. (Segunda communicación.)—*Medicina de Hoy*. Habana. 1936. Sept. Vol. 1. No. 8. pp. 313–318. With 2 figs.

[8] BAKER (J. N.), MCALPINE (James G.) & DOWLING (J. D.). Rabies: a Continuing Challenge.—*Southern Med. Jl.* 1936. June. Vol. 29. No. 6. pp. 547–555. With 7 figs.

[9] NICOLAU (S.) & KOPCIOWSKA (L.). Passage en série, de nerf à nerf, chez le lapin, du virus rabique fixe; récupération de la "negrigenèse."—*C. R. Soc. Biol.* 1936. Vol. 122. No. 18. pp. 280–282. With 1 fig.

[10] MILLISCHER (P.) & MILLISCHER (A.). Expertise du virus rabique fixe utilisé à Beyrouth.—*Bull. Soc. Path. Exot.* 1936. June 10. Vol. 29. No. 6. pp. 626–632.

[11] LÉPINE (P.) & SAUTTER (V.). Aptitude negrigène du virus fixe de Sassari.—*C. R. Soc. Biol.* 1936. Vol. 122. No. 20. pp. 542–544. With 2 figs.

animals. The authors find that numerous well developed Negri bodies appear in the usual situations in rabbits inoculated with the Sassari fixed virus. It thus behaves with regard to negrigenesis as a street virus. Its characters have not changed during 1,700 subpassages occupying a period of 36 years. But initially the Sassari strain emanated from Paris. It was introduced into Sassari in 1900, and after 25 to 26 passages it had increased in virulence not only for the rabbit but for the mouse. It now differs profoundly from the parent strain. There has been no parallelism between the two collateral branches of the same fixed virus, that subpassaged in Sassari and that subpassaged in Paris.

Using graded collodion membranes for ultrafiltration Galloway and Elford[12] record results as to the dimensions of rabies fixed virus (Paris strain). As the result of a series of experiments they find that active filtrates were obtained after filtration through membranes of porosities varying from 0·5μ to 0·25μ. "Even under the most favourable conditions, no virus was detected in filtrates from membranes of A.P.D. 0·2μ, and this porosity is therefore taken as the filtration end point." This leads the authors to "assign a value of 100–150 mμ for the particle diameter of the virus of rabies." This result is in accordance with that reported by Yaoi, Kanazawa and Sato (this *Bulletin*, 1936, Vol. 33, p. 743), who found that the end point for a Japanese strain of fixed virus was also 0·2μ.

In a second paper, Elford and Galloway[13] deal with the dimensions of Aujeszky's virus. The end point in this case is also 0·2μ indicating a particle size of the virus of 100–150 mμ.

From experiments conducted by Jonnesco,[14] it appears that pancreatic juice in a dilution of 1 in 10 may destroy rabies virus, but the effect is variable. This action is stated to be due to the action of the tryptic ferments of the juice, as if these all neutralized by the antitryptic ferments of normal serum, there is no longer any indication of destructive action.

From experiments carried out by MacKay and Schroeder[15] it appears that aequeous solutions of urea kill the rabies virus with ease. Two rabbits given 0·1 and 0·2 cc. of untreated virus suspension intracerebrally died with incubations of 6 and 8 days respectively. Of 4 rabbits inoculated by the same route with 0·1 up to 0·3 cc. of urea treated rabies virus none developed the disease. The urea treated virus contained 50 per cent. of cord-brain, and 40 per cent. of urea.

ii. *Symptomatology.*

A case of paralytic rabies in which the interval between onset of symptoms was much prolonged (22nd January till 4th February) is

[12] Galloway (I. A.) & Elford (W. J.). The Size of the Virus of Rabies ("Fixed" Strain) by Ultrafiltration Analysis.—*Jl. Hygiene.* 1936. Oct. Vol. 36. No. 4. pp. 532–535. [11 refs.]

[13] Elford (W. J.) & Galloway (I. A.). The Size of the Virus of Aujeszky's Disease ("Pseudo-Rabies," "Infectious Bulbar Paralysis," "Mad-Itch") by Ultrafiltration Analysis.—*Jl. Hygiene.* 1936. Oct. Vol. 36. No. 4. pp. 536–539. [13 refs.]

[14] Jonnesco (Démètre). Action du suc pancréatique (homme) sur le virus rabique.—*C. R. Soc. Biol.* 1936. Vol. 123. No. 26. pp. 43–46.

[15] MacKay (Eaton M.) & Schroeder (Charles R.). Virucidal (Rabies and Poliomyelitis) Activity of Aqueous Urea Solutions.—*Proc. Soc. Experim. Biol. & Med.* 1936. Oct. Vol. 35. No. 1. pp. 74–76.

reported from Saigon by VAUCEL and HOANG-TICH-TRY.[16] The course of the disease was in all respects similar to that of a previous case at Saigon described by DOROLLE, CHAUSSINAND and TRAN-VAN-TAM (this *Bulletin*, 1935, Vol. 32, p. 608.). The diagnosis of rabies was confirmed both microscopically by the presence of Negri bodies, and by animal inoculation. The affection commenced on 22nd January with fever, anxiety and headache. On the 26th weakness of the upper limbs was observed. Thereafter the course was that of an ascending paralysis.

A case of hydrophobia which at the onset showed the symptoms of a transverse myelitis is reported by ROY.[17]

A case of rabies which occurred on the 12th day after completion of a course of treatment by Semple's method is described by GUPTA.[18] It was first diagnosed as a post-vaccinial paralytic accident, but later the usual symptoms of rabies developed.

iii. *Pathology.*

MANOUÉLIAN[19] extends his observations on alterations in the nerve cells in rabies (this *Bulletin*, 1936, Vol. 33, p. 320). Neurons during the course of infection show marked alterations, and are ultimately destroyed and disappear. A large number of nerve cells are encroached upon by satellite cells. These proliferate and finally occupy the space of the original neurone, thus forming the nodules of van Gehuchten. But where hypertrophy of the neurofibrils has occurred this is not the case. It appears that the neurofibrillary network strongly resists destruction.

LEVADITI and SCHOEN[20] report further observations on the presence of negri bodies in the corneal epithelium. It appears that in corneal epithelium, regenerated after previous destruction by croton oil, or radiation by a mercury vapour lamp, negrigenesis occurs more actively and more constantly than in normal corneal epithelium, whether the infecting dose of rabies virus is given by scarification of the cornea, or intracranially. They add that they have found negri bodies in cells of the corneal epithelium which are in the stage of mitosis, which proves that the rabies infection does not hinder karyokinesis.

iv. *Methods of Treatment.*

A very important pronouncement is made by REMLINGER and BAILLY[21] in a contribution presented to the Academy of Medicine. They commence by quoting from a letter from Pasteur to Duclaux. "The interest which vaccination with *non virulent* medulla would

[16] VAUCEL (M.) & HOANG-TICH-TRY. Évolution lente d'un cas de rage paralytique.—*Bull. Soc. Méd.-Chirurg. Indochine*. 1936. June. Vol. 14. No. 6. pp. 681–684.

[17] ROY (A. C.). Hydrophobia simulating Acute Transverse Myelitis at the Onset.—*Indian Med. Gaz.* 1936. June. Vol. 71. No. 6. p. 339.

[18] GUPTA (S. C. Sen). A Case of Paraplegia and Hydrophobia following a Full Course of Anti-Rabic Treatment.—*Indian Med. Gaz.* 1936. Nov. Vol. 71. No. 11. p. 660.

[19] MANOUÉLIAN (Y.). Nodules rabiques et réseau neurofibrillaire.—*C. R. Soc. Biol.* 1936. Vol. 123. No. 29. pp. 494–496. With 3 figs.

[20] LEVADITI (C.) & SCHOEN (R.). Négrigenèse cornéenne et régénérescence épithéliale.—*C. R. Soc. Biol.* 1936. Vol. 122. No. 21. pp. 616–618.

[21] REMLINGER (P.) & BAILLY (J.). Contribution à l'étude de la vaccination antirabique par les vaccins phéniqués.—*Bull. Acad. Méd.* 1936. June 9. 100th Year. 3rd Ser. Vol. 115. No. 22. pp. 788–793.

excite need not be emphasized. It would be a scientific fact of the first order, and an inestimable advance in the method of prophylaxis of rabies." The authors continue: "Vaccination by dead virus was foreseen by Pasteur himself, was instigated by him. It results directly from his immortal discovery." "It is only just to recall that the honour of the first application of phenol to the attenuation of rabies virus belongs to Fermi, and that vaccination by phenol vaccines is inseparable from his name." A description of the virus employed by the authors is then given. It is a 5 per cent. emulsion, containing 1 per cent. phenol, filtered through gauze, and then heated at 37°C. for 24 hours. It is a Semple vaccine. "We should note that if the percentage of phenol is less than 0·75, and if incubation at 37°C. for 24 hours is not carried out, the vaccine is capable of infecting a rabbit, when ½ cc. is injected subdurally. Does this imply that when inoculated under the skin of man or dog there would be danger of infection? Far from it. We are persuaded that the contrary is the case. Nevertheless, in countries such as Africa and Western Europe, where rabies virus has usually only a feeble aggressibility it appears preferable for human vaccination at least, only to employ vaccines which have been rigorously killed."

The authors then relate certain comparative experiments carried out by themselves on rabbits, dogs, and an ass, of which the results were satisfactory. They then quote the reviewer's finding from the statistics furnished to the League of Nations, that no superiority of living over dead vaccines could be detected. This, they continue, is in agreement with their experimental results. They then compare cord and killed phenol methods of treatment categorically and in detail, and conclude "these experiments and the statistics furnished from the numerous institutes, even for wolf bites, ought to attract serious attention. No method of vaccination is more practical and better adapted to the necessities of modern life." This paper is of far-reaching importance, and should be read in the original. It would appear that the efforts of the Health Section of the League of Nations in summoning a Conference in 1926, at which a large mass of evidence was put forward, and in collecting statistics during the succeeding years, have not been in vain. It is to be hoped that this decision of Remlinger's will clarify the situation, and that his aspiration that the treatment of rabies may be standardized will take concrete form in the near future. As the reviewer has so often emphasized, the treatment of rabies by fixed virus, in whatever form it may be exhibited, is the treatment of Pasteur.

An experiment on the comparative immunizing powers of Fermi's original carbolized vaccine (*i.e.*, kept for 24 hours at 20°C.) and Semple's modification (*i.e.*, kept for 24 hours at 37°C.) has been carried out by Mulas.[22] The result may be summarized as follows:—

Of 18 rabbits which had received an infective dose of 0·25 cc. of Sassari virus subcutaneously and were treated by Semple's method (2 to 4 cc. of a 5 per cent. vaccine daily) commencing after intervals of one, three and five days, one survived (*i.e.*, 5·5 per cent.).

Of 18 rabbits similarly treated by Fermi's vaccine, 10 survived (*i.e.*, 55·5 per cent.)

Of 8 untreated rabbits none survived.

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[22] Mulas (F.). Valeur comparée de la méthode de Fermi et des autres vaccins phéniqués pour la vaccination antirabique. Inefficacité des modifications apportées à la méthode originale.—*Rev. d'Hyg. et de Méd. Préventive.* 1936. June. Vol. 58. No. 6. pp. 419–426.

From this result the author claims that the Semple modification is only one-tenth as effective as Fermi's original method. He quotes also the figures of an early experiment on the same point by Fermi himself (for the figures see this *Bulletin*, 1928, Vol. 25, p. 711), but in this case the contrast was not so striking, the relative efficiencies of the two vaccines being of the order of 6 to 10. What is essentially the same paper appears in an Italian Journal,[23] with a slight and somewhat naive change of title.

A slightly different experiment on the same subject was carried out by COVELL, MCGUIRE, STEPHENS and LAHIRI.[24] In this case the treatment was pre-infectional. Duplicate vaccines were prepared, of which one was incubated at 37°C. for 24 hours and the other was kept at room temperature. 30 monkeys were immunised with incubated virus, and 30 with unincubated. Both groups received a daily dose of 2 cc. of 5 per cent. emulsion for 14 days, and 3 weeks after completion of treatment the monkeys of both groups together with 30 untreated monkeys received an infecting dose of 2 cc. of a 2 per cent. emulsion of street virus in the muscles of the neck. The result was as follows:—

Of 25 monkeys treated with incubated vaccine none died of rabies.

Of 27 monkeys treated with unincubated vaccine none died of rabies.

Whilst of 36 untreated, 11 died of rabies.

The experiment was repeated with the following result:—

Of 39 monkeys treated with incubated vaccine one died of rabies.

Of 39 monkeys treated with unincubated vaccine none died of rabies.

Of 40 untreated monkeys 23 died of rabies.

From these results the authors conclude that "no significant loss in efficiency is produced by incubating carbolized 5 per cent. antirabic vaccine at 37°C. for 24 hours." It is to be noted that in the experiment carried out at the Indian Laboratory the treatment was pre-infectional, whilst in that carried out at Sassari it was post-infectional. In spite of this difference, however, it seems difficult to reconcile the two results.

A further series of experiments by COVELL and his co-workers was carried out to elucidate the question as to whether antirabic serum as an adjunct to treatment by carbolized vaccine increased protection. Though carried out on a large scale (260 monkeys) the results were inconclusive.

The authors quote the results of a similar test on human cases carried out by SHORTT, MCGUIRE, BROOKS and STEPHENS (this *Bulletin*, 1935, Vol. 32, p. 610), from which they conclude that the results "suggest that antirabic serum adds to the value of carbolized vaccine in preventing the onset of rabies, but many more cases must be treated before a definite opinion can be expressed on this point."

[As remarked, in reviewing that paper, the results do not indicate a significant difference between the two methods of treatment.]

In the second section of their paper they show that the immunizing value of carbolized vaccine prepared from the spinal cords of sheep is very much less than that prepared from the brain.

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[23] MULAS (F.). Dannose ed assurde modificazioni inglesi al metodo antirabbico Fermi.—*Boll. Istituto Sieroterap. Milanese.* 1936. Sept. Vol. 15. No. 9. pp. 576–580. French summary.

[24] COVELL (G.), MCGUIRE (J. P.), STEPHENS (E. D.) & LAHIRI (B. N.). Notes on Antirabic Immunization.—*Indian Jl. Med. Res.* 1936. Oct. Vol. 24. No. 2. pp. 373–388.

In a third section of this paper it is shown that of 70 guineapigs inoculated subdurally with 0·2 cc. of seven samples of Semple's vaccine selected at random from stock, none developed rabies. Thus the vaccine employed at Kasauli contains only dead virus.

In their fourth section they show that the immunizing properties of the Kasauli vaccine are retained unimpaired for 7 months, in the ice chest.

A further section deals with the correlation between complement fixation tests and immunity to rabies. The sera of 131 monkeys (survivors from a previous experiment) after a 6 months' interval were examined for complement fixation. These monkeys were then given a second infecting dose to test their resistance. The results were as follows :—

Complement fixation.	*Number of Sera.*	*Deaths.*
Strong positive ...	36	5
Weak positive ...	38	2
Incomplete ...	16	1
Negative	41	6
	131	14

From this result they conclude that " the complement fixation test is not an accurate means of gauging immunity response in connection with antirabic treatment."

In a final section they state that they have been unable to detect any superiority of virus fixed in the dog, over virus fixed in the rabbit or sheep, in the protection of dogs from rabies (*cf.* Jonnesco this *Bulletin*, 1933, Vol. 30, p. 142).

Using antisera prepared from rabbits and goats, Hoyt, Fisk, Moore and Tracy[25] have conducted a series of experiments upon the passive immunization of rabies. When large intraperitoneal injections of antiserum were given before intracerebral virus inoculation, a higher percentage of 188 treated mice (36 per cent.) survived than of the 247 corresponding controls (9 per cent.), and in addition the mean incubation period was lengthened by the treatment. When antisera were given 16 days before or shortly after the infecting dose there was no evidence of protection. When on the other hand the sera were given intracerebrally half an hour before an intracerebral infecting dose protection was marked (19 out of 26 mice survived, as compared with 5 out of 59 controls). But when given either 24 hours before or 2 hours after, it was ineffective.

Using their " protection test " previously described in these reviews (this *Bulletin*, 1935, Vol. 32, p. 178) Reichel and Schneider[26] report experiments which show that resistance against rabies infection is increased after treatment by killed phenol rabies vaccines, as compared with phenolized normal brain substance.

[25] Hoyt (Anson), Fisk (Roy T.), Moore (Frederick J.) & Tracy (Ralph L.). Experimental Rabies in White Mice II. Studies on Passive Immunization.—*Jl. Infect. Dis.* 1936. Sept.–Oct. Vol. 59. No. 2. pp. 152–158.

[26] Reichel (John) & Schneider (J. E.). Response to Rabies Vaccine Prophylaxis as shown by Protection Tests.—*Amer. Jl. Public Health.* 1936. Aug. Vol. 26. No. 8. pp. 789–792.

Of 510 persons treated at the Pasteur Institute of Paris[27] during the year 1935, none developed rabies.

Symptoms and pathological appearances of a case of paralytic accident of the Landry type are described by Ch'en and Ch'eng.[28] These were of the usual type, and the authors state that their histological findings were indicative of a toxic degenerative process.

v. *Rabies in Animals.*

The rôle of wild carnivora in the transmission of rabies was discussed by Thomas and Neitz[29] at the South African Health Congress, held at Cape Town in February, and the question of the possibility of controlling the prevalence of meerkats was considered.

The work of Remlinger and Bailly[30] on the transmission of rabies to various birds is well known. They now report observations of rabies in the stork (*Ciconia ciconia*). Using street virus they have been able to transmit the disease to two storks by subdural inoculation. The symptoms were those of paralytic rabies, without any indication of excitability. Diagnosis was confirmed by animal inoculation.

vi. *Miscellaneous.*

In continuation of former work on fixed virus (this *Bulletin*, 1936, Vol. 33, p. 751) Yen[31] shows that the Chinese hamster is also susceptible to street virus.

Millischer and Marteau[32] report that in certain experiments carried out with cords, dried for 2 days, and subsequently kept at 7°C. in the ice chest for periods varying from 12 to 158 days, a large proportion of the rabbits inoculated exhibited symptoms of excitability, approaching sometimes to fury.

Tyndel and Pasternak[33] have failed to find confirmation of Nikolić's assertion (this *Bulletin*, 1936, Vol. 33, p. 326) that antirabic vaccines can be used with hope in cases of epilepsy. They used it on 10 cases without result. *A. G. McKendrick.*

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[27] Viala (Jules). Les vaccinations antirabiques à l'Institut Pasteur en 1935.—*Ann. Inst. Pasteur.* 1936. June. Vol. 56. No. 6. pp. 717–721.

[28] Ch'en (M. P.) & Ch'eng (Y. L.). A Case of Acute Ascending Paralysis Complicating Anti-Rabic Treatment.—*Chinese Med. Jl.* 1936. May. Vol. 50. No. 5. pp. 683–686. With 2 figs. on 1 plate. [11 refs.]

[29] Thomas (A. D.) & Neitz (W. O.). Wild Carnivora as Carriers of Rabies.—*Jl. Roy. San. Inst.* 1936. June. Vol. 56. No. 12. pp. 754–760.

[30] Remlinger (P.) & Bailly (J.). Transmission de la rage à la cigogne (*Ciconia ciconia*).—*C. R. Soc. Biol.* 1936. Vol. 123. No. 28. pp. 383–385.

[31] Yen (Albert C. H.). Experimental Virus Infections in Chinese Hamster. II. Susceptibility to Street Rabies Virus.—*Proc. Soc. Experim. Biol. & Med.* 1936. June. Vol. 34. No. 5. pp. 648–651.

[32] Millischer (P.) & Marteau (P.). Observations sur la congélation des moelles rabiques.—*C. R. Soc. Biol.* 1936. Vol. 122. No. 22. pp. 727–728.

[33] Tyndel (M.) & Pasternak (M.). Zur Behandlung der genuinen Epilepsie mit antirabischen Vakzinen.—*Wien. Klin. Woch.* 1936. Aug. 14. Vol. 49. No. 33. pp. 1017–1018.

MISCELLANEOUS.

SMIT (H. P.). **Climate in South Africa.**—*South African Med. Jl.* 1935. Nov. 23. Vol. 9. No. 22. pp. 782–789.

This is a fairly detailed discussion on climatic conditions in South Africa as a whole and on climatic variations between different parts of the Union in particular. The maps and graphs described in the paper have been omitted as they have been published previously in the Year Book of the Union.

One of the author's objects is to point out the great variety of climates which occur in the Union of South Africa and to suggest the possibility of establishing new health resorts and centres for the treatment of diseases, should the need for these be indicated by the medical profession.

In addition to latitude the three principal climatic influences are: (1) the relative distribution of land and sea; (2) altitude above sea level and general topography; (3) ocean currents.

Conditions on the east and west coasts of South Africa form a striking contrast on account of the warm Mozambique current on the east coast and the cold Benguela current on the west.

The high temperatures associated with low latitudes are in South Africa generally offset by a considerable altitude above sea level. Rainfall, though heavy in parts of the Union, may be said to be less effective than rainfall in Great Britain on account of the heaviness of the showers and the hot dry periods between them. Mean temperatures, contrary to general opinion, do not vary very greatly from those found in England, but the diurnal temperature range is considerable.

The author concludes that the diversity of South African climates calls for more adaptation in diet, clothing and housing conditions, which European conservatism finds hard to adopt. He considers the white population to be too much ruled by European conventions to enjoy to the full the usually healthy climate in South Africa.

T. C. Angus.

ANNING (C. C. P.). **Tropical Sanitation: the Town.**—*Jl. Roy. San. Inst.* 1936. June. Vol. 56. No. 12. pp. 787–800. [Summary appears also in *Bulletin of Hygiene.*]

The present and future public health problems in towns of the tropics and subtropics of Africa concern the non-white sections of the population, and the education of this section is best done by well trained people of the same colour and social background. The interdependence of the white and other races in the town, and that of the town and country is illustrated by reference to the vital statistics of Pietermaritzburg. While only about 15 per cent. of white deaths are put down to preventable disease, 50 per cent. of non-white deaths are attributed to such disease. Since February 1934 all male natives entering the town have been medically examined and up to November 30th, 1935, 3·97 per cent. were refused registration on account of infectious disease, mostly venereal disease or tuberculosis.

A housing survey showed that of all houses marked for demolition on account of their insanitary state only one per cent. were occupied by whites, although the white and non-white populations are equal. Several reasons are given to explain why it is that the rural native tends to become a slum dweller on entering a town, and requires

re-education in hygienic principles to meet his altered environment. The town owes a good deal of its disease to incomers from the rural areas around; these may be human carriers of disease, and such things as rodent carriers of plague, or the insect vectors of malaria.

As regards the last point it is remarked that prior to 1929 *Anopheles costalis* was not reported in the town, but thereafter it and malaria occurred annually, in increasing amount from January to May, till 1932 when action was taken. The steady advance of *costalis* up the river into the town from the rural areas lower down and nearer the coast, is illustrated by a table giving dates of capture of anophelines and cases of malaria. The adult anophelines were discovered in huts by the use of insecticides a week before larvae could be found by intensive search for breeding places.

Nine cases of typhus, attributed, with some reserve, to flea agency, were found in the town during the year.

The Pietermaritzburg Municipal Native Village points the way to the solution of the greater part of the native disease problem; brick buildings each with its own garden, proper sanitation, purified water supply, adequate ventilation and sunshine inlet, with washing areas, and a controlled market. *D. B. Blacklock.*

Ross (G. A. Park). **Tropical Sanitation in its Application to Native Reserves.**—*Jl. Roy. San. Inst.* 1936. June. Vol. 56. No. 12. pp. 801–806. [Summary appears also in *Bulletin of Hygiene.*]

Dr. Ross insists that disease prevention in native areas is not effected by providing medical aid; the public health needs of towns are not met by practitioners, hospitals, clinics and dispensaries, and what applies to towns applies equally to the country. In the native reserves organization under his control, the duties which would ordinarily fall to a European sanitary inspector in a European area, are done by educated natives, while the supervising and organizing duties of a head inspector are done by European sanitary inspectors under the medical officers. The author found that the Zululand natives could be educated to the extent of believing that lice are responsible for their typhus, and of washing themselves as required. In Natal the Berg people are dirty and have much typhus, but he finds that they can be taught by educated people to rid themselves of lice. Trained members of the native staff, living with native chiefs, can induce the natives to deal with outbreaks themselves, naphthalene oil and soap being distributed in convenient places. The author is optimistic as to the prospects of education in hygiene and disease prevention in these native areas. *D. B. Blacklock.*

Orenstein (A. J.). Tropical Sanitation in its Application to Organised Industry in South Africa.—*Jl. Roy. San. Inst.* 1936. June. Vol. 56. No. 12. pp. 777–786.

Werner (H.). Zur Frage der Akklimatisation der Weissen im tropischen Hoch- und Tieflande. Deutsche Siedlung in Espirito Santo (tropisches Brasilien). [**Adaptation of the White Man to Tropical Climates. Germans in Espirito Santo.**]—*Deut. Med. Woch.* 1936. Aug. 7. Vol. 62. No. 32. pp. 1304–1306.

The tropical regions include 45 per cent. of the total of the earth's surface and the question is raised as to whether they should be regarded

any longer as unsuitable for the white race on account of climate and unhealthy conditions. It is pointed out that this is a matter of very great interest to Germany in view of future colonial expansion.

Particular attention is called to two German colonies which were established in Espirito Santo, a State on the coast of Brazil between Bahia on the north and Rio de Janeiro on the south. One of these colonies was formed by a group of 38 families numbering 163 persons from the Rhineland who landed at Victoria, the chief port of the State, in 1847. They went inland partly on foot and partly by canoe and after clearing the ground settled. During the next few years they received additions from Germany. In 1855 a private company sent out 1,000 persons consisting of Germans, Swiss and Tyrolese, who formed the colony of St. Leopoldina. In 1915 the total numbers of these two colonies was 17,000 to 18,000, which had developed in three generations from between two and three thousand immigrants. The increase was found to have taken place in the lowlands as well as the highlands. The employment was mostly growing maize and coffee, rearing cattle and breaking up new ground. It was found that work could be carried on for eight hours a day with a long rest midday. There was a system among these colonists called "Bittarbeit" under which if one of them wished to build a house or undertake some work which was beyond him he could ask the assistance of his neighbours and this had to be given without pay, but similar help would be given in return when required.

Malaria, yellow fever, enteric, dysentery and hookworm disease were effectively dealt with, but many women died in childbirth. Snake bites and accidents in the forests were among the causes of death.

The constitution of the colonist was found to have in no way deteriorated after several generations. They were of good physique and retained their German characteristics. *A. J. Collis.*

Peacock (W. H.). **Presidential Address on the Training and Place of Auxiliary Health Staff in Tropical Colonies.** –*Jl. Roy. San. Inst.* 1936. Nov. Vol. 57. No. 5. pp. 299–305.

Dr. Peacock writes from his experience in two African colonies, Sierra Leone and Nigeria. In tropical Africa it would be far too costly to employ more than a nucleus of Europeans on the medical and sanitary staff. In Nigeria, for example, with a population of 20,000,000, the total strength of the Colonial Medical Service does not exceed a hundred. It will be necessary for many years to maintain some European health officers and sanitary inspectors for administration and for supervision and training of an African staff.

In Lagos there has existed for years a centre for training African sanitary inspectors for service with the Government and the local town council and a few for native administration areas. Their syllabus is a wide one and includes instruction in parasitology, entomology, communicable and epidemic disease, disinfection, disposal of refuse and night-soil, drainage, water supplies, ventilation, rat destruction, meat and food inspection, village sanitation, vaccination, clerical duties in keeping records and vital statistics, also elementary meteorology, police court duties and sanitary law.

The fact has been realized for some time that one training centre was not enough and schemes have been approved for three more—one for the Northern Provinces at Kano, and two for the Southern Provinces,

one at Ibadan (for Yoruba provinces), the other at Umuahaia (Owerri Province, for the Ibo and Effik districts). The last was opened in 1934.

Native administration inspectors are engaged chiefly in the work of rural sanitation—in the network of native administration village dispensaries which, in recent years, have sprung up all over Nigeria. By the end of 1934 there were 231 of these dispensaries, 96 in the Northern and 135 in the Southern Provinces. They are staffed by dispensary attendants trained at the larger hospitals. They provide the people with simple treatment, medical and surgical, and so gain their confidence. The idea is to make them in time real local health centres and to provide a full health staff of sanitary inspectors, vaccinators, midwives and health visitors.

In 1930 a school of medicine was established at Lagos on the lines of those at Mulago and at Khartoum. After a course of 5 years, two devoted to clinical work, approved candidates receive certificates entitling them to practise medicine, surgery and midwifery in the Government service. When a "medical assistant," as he is then called, has been registered for at least 3 years, one of which has been spent in an approved course of special study, and has passed a further examination, he is granted a diploma which entitles him to be called a Licentiate of the School of Medicine, and he may then be placed on the local register as a medical practitioner.

The course for students of the Lagos Health Department in public health, tropical hygiene and infectious diseases is very thorough and these students are likely to play an increasing part in public health work in Nigeria. A certain proportion of them will be available for rural health work in the dispensaries and they will act as house surgeons at the hospitals and so set free the European medical staff for health work in their districts.

The training of midwives is all-important and doubtless thousands of lives could be saved by antenatal care and proper midwifery. The Midwives Ordinance of Nigeria (1930) recognizes two grades: Grade I. Certificated women who have undergone a course of training in nursing and midwifery for at least 2½ years in an approved school. The first six months are spent in a preliminary course in general nursing at an African general hospital, after which training at a recognized midwifery training centre begins. Grade I certificate holders can practise midwifery anywhere in Nigeria. Grade II are partially trained midwives, of illiterate type. Their training is obtained at mission hospitals recognized by the Midwives Board. This period of training is at least six months; their examination is oral and practical only. Those who pass are registered for practice only in the area where they were born or have resided for not less than ten years. It is hoped that they will displace the "Mother Gamp" type practising in rural districts to the no little danger of the community. *H. H. S.*

Blacklock (Mary G.). **Certain Aspects of the Welfare of Women and Children in the Colonies.**—*Ann. Trop. Med. & Parasit.* 1936. July 17. Vol. 30. No. 2. pp. 221–264. [Summary appears also in *Bulletin of Hygiene.*]

It is impossible in a brief summary to do justice to this long and important paper, which should be read in the original by all who are

interested. It was written after a visit to the East as the holder of a Leverhulme Fellowship. The author has also had considerable experience of health work amongst women and children in India and West Africa.

Early activities in the colonies during the stage of development were chiefly the concern of men. Consequently the first schools and hospitals were almost exclusively for males. Missionaries did something to redress the balance, as the women Missionaries took part in the education and medical care of women and girls. This paper describes the present position in the colonies, draws attention to some unsatisfactory aspects and makes suggestions for improvements. An account is given of certain recent developments for the training of health visitors, nurses and midwives.

While the general standard of medical work in most of the colonies is high, this is by no means always the case as regards women and children. There is often a grave disproportion between the number of male and female patients receiving treatment at the hospitals. There are Mohammedan districts in which no woman medical officer is employed. Welfare work is sometimes left mainly to voluntary effort.

Native women are apt to be frightened by the officialdom of large hospitals and the appointment of women as reception clerks is recommended.

Dissociation of welfare work from hospital work is often a cause of failure.

The education of girls and women from a public health point of view is discussed and the author commends the Jeanes system of education for villages in primitive communities. By this method the teacher and his wife receive practical health training and are then posted to a village in which they are expected to raise the standard of the community by example and precept.

An account is given of an interesting school in Nigeria in which girls of marriageable age are given practical training in domestic economy and hygiene under village conditions together with a little elementary education.

Greater attention should be devoted to training native women teachers, especially in the practical study of health problems and their solution, and more time should be given to the teaching of hygiene, domestic science and mothercraft in girls' schools.

Wireless broadcasting will play an important part in the future in the education of women in the villages.

Organizations for women are needed to take the place of the original tribal societies in which women have always played a prominent part. Women's branches of co-operative societies may be used for this purpose.

In many colonies better planned efforts are needed for the training of nurses, midwives and health visitors, and two grades may be necessary. An important activity of the welfare centres should be to train and supervise uneducated local women for these purposes. More women doctors are needed in the colonies and women should be appointed as special advisers on medical work for women and children. Local women should also be trained as medical assistants or doctors.

In every colony there should be some organization charged with the welfare of women and children to study social problems affecting them.

W. H. Peacock.

Henry Lester Institute of Medical Research. **Annual Report 1935.**—86 pp. With 9 figs. on 5 plates. 1936. Printed by N.C.D.N. Shanghai.

This report records a year of much activity. No fewer than 75 publications are listed in the Appendix and only a fraction of the work can be noticed here. The Introduction indicates its scope. In the Clinical Division the study of beriberi has been continued and in that of Physiological Sciences factory diets. "Dr. Read and his colleagues have shown through their analysis of the vitamin content of Chinese food that instinct and custom when not interfered with by modern civilization provide an adequate amount of these necessary dietetic principles." [Though this would appear obvious there are, it seems, authors who think otherwise.] In the Division of Pathological Sciences an advance has been made in the analysis of the antigenic structure of the typhoid bacillus and in the preparation of a serum for treatment. Dr. Maxwell has done valuable work on leprosy. This Division conducts field investigations, especially in entomology and parasitology and the section on Field Medical Research in China is particularly interesting. In this part of China there is a huge fertile alluvial plain, intensively cultivated for generations. It is intersected by a network of waterways most of which are navigable by the countless small craft of the region. A vast population spends its entire existence afloat and the waterways abound in fish, crustaceans and molluscs, most of which are used for food. The situation favours mosquito breeding and malaria and filariasis are prevalent. The return of excreta to the soil keeps many helminthic diseases going such as schistosomiasis japonica, paragonimiasis and fasciolopsiasis.

Extracts from a collecting trip diary give an idea of the work that is being undertaken.

The Department of Epidemiology and Medical Statistics has concerned itself with the analysis of in-patient and out-patient records provided by the hospitals co-operating in the Chinese Medical Association Hospital Survey; in 1934 malaria was one of the major causes of morbidity. An investigation of printing works showed that conditions were bad and it was concluded that industrial hygiene is "almost hopeless of attainment in the absence of government regulation of industry." The Division of Clinical Research and Experimental Surgery has made considerable progress in the study of disordered nutrition as seen in the beriberi syndrome. An important chemical change in the blood is the accumulation of carbonyl compounds, especially of pyruric acid, the amount of which may be determined from the bisulphite binding capacity and follows the degree of Vitamin B_1 deficiency as determined by clinical criteria. A practical indication from the work is that enormous doses of Vitamin B_1 are required for effective treatment in the more severe grades of B_1 deficiency.

The Division of Physiological Sciences has concentrated upon nutrition problems—Chinese diets and the vitamin content of Chinese foodstuffs.

The Division of Pathological Sciences has directed its attention to the local diseases or the parasites which cause them. In the work on the sero-diagnosis of typhoid it was found that the standard Widal technique using "H" suspensions alone may lead to an erroneous positive in nearly 20 per cent. of cases, and it is important that "O" antigen be used, especially where facilities for blood culture are lacking. A new

curative serum was prepared, based on the finding of a new " Vi " antigen in *Bact. typhosum* ; 24 cases have been treated with encouraging results.

A large amount of section cutting was done for hospitals outside Shanghai. From the results of the examination of livers from cases of splenomegaly at Foochow it is believed that schistosomiasis is here in question, which would be a new record for this infection. A search is to be made for infected molluscs.

The writer points to the possibility of destroying the fecundity of Oncomelania snails by means of single-tailed cercariae, which is being explored. In the work on filarial transmission it was found that matured filarial larvae in mosquitoes infected in the latter part of the autumn were not able to survive the winter in their hosts. A tabulated record of the examinations made at the Institute concludes the Report.

A. G. Bagshawe.

KENYA COLONY AND PROTECTORATE. **Medical Research Laboratory Annual Report, 1935** [CORMACK (R. P.), Senior Bacteriologist].—27 pp. 1936. Nairobi : Govt. Printer.

This report indicates that heavy routine demands were made upon all divisions of the Institute.

Research has included the typing of pneumococci, with prophylactic and therapeutic tests of pneumococcal vaccines specially prepared for local use. The records, given in brief, are so far inconclusive.

In an intensive investigation of the South Kenya endemic plague area, no evidence was found that plague existed in the *field* rodents, nor that any spread was occurring from that area. It has been noted that in the native reserves the rats, which live chiefly in the thatched roofs of the huts and therefore do not need to enter the hut in order to reach the villagers' cereal stores outside, harbour *X. brasiliensis* only. This has been deduced, no doubt correctly, to be a factor associated with the lower human mortality in plague outbreaks in native reserves compared with that in urban areas. In the townships, although the rats as a whole harbour a mixed flea population, many rats live underground, and these have been found to be infested with *X. cheopis* only. Such rats, and therefore fleas too, come into closer contact with the human inmates of the dwelling than do those in the native reserves.

A survey of the Colony as regards its schistosome-carrying snails has been started.

Epidemiological, clinical and serological features of " Tropical Typhus of Kenya " have been found to correspond very closely with those of " fièvre boutonneuse." Examination of the blood of 74 normal persons has demonstrated that the haemoglobin content shows an increase to be expected from the altitude of residence above sea-level, " but this has not in general been accompanied by an increase in cell count."

P. H. Martin.

CRUICKSHANK (Alexander). **Tropical Diseases of the Southern Sudan : their Distribution and Significance.**—*East African Med. Jl.* 1936. Sept. Vol. 13. No. 6. pp. 172–177.

The country in question lies to the south of 10° N. lat. and is peopled by negroid tribes ; the population is 1½ millions and the area 200,000 square miles.

Malaria, chiefly malignant tertian, is universal (splenic index 90–100 per cent.), blackwater fever is sporadic. *Human trypanosomiasis* occurs along the south-western border where French Equatorial Africa and Belgian Congo lie; last year 92 cases were diagnosed. *Yellow fever.*—One case has been recognized and the mouse protection test showed 17 out of 30 to be positive at Rumbek and a smaller proportion elsewhere. *Amoebic dysentery* is widespread, liver abscess rare. *Leprosy* is rare in the north-east among the cattle owners, and common in the great fly belt, 98 in 950,000 as against 6,944 in 643,000. A census of the Zande tribe showed 3·9 per cent. to be infected. There are now 2,368 lepers in 11 settlements. *Yaws* has much diminished owing to energetic treatment; it is still prevalent in remoter areas.

Of helminthic infestations: *Schistosomiasis mansoni* is common in the south-west and of mild type. Seventeen per cent. of admissions at Li-Rangu harboured this parasite. *Filariasis.*—The forms recognized are *A. perstans*, *Loa loa* and *O. volvulus*. *Loa loa* is found in the country bordering French and Belgian territory; at Li Rangu hospital 38 per cent. of 681 male hospital admissions and 20 per cent. of 369 female admissions harboured this parasite. *O. volvulus* has a wider distribution and produces subcutaneous nodules, skin eruptions, elephantiasis of the genitals, hydrocele and eye lesions, including total blindness. *Dracontiasis* is found patchily over most of the area. Prophylactic measures in the Yei district have almost banished it. An emulsion of the local heglig berries (*Balanites*) is used for killing cyclops in wells and pools. *Ankylostomiasis* is "reaching serious proportions," affecting the whole area west of the Nile. Among the Dinka herdsmen anaemia, ascites and other symptoms are seen. *Hydatid* disease occurs on the Abyssinian border.

Tropical sloughing phagedaena affected 60–70 per cent. of over a million out-patient attendances. The author has little doubt that dietary deficiency is the main predisposing cause. After thorough cleansing bandages soaked in the ordinary gum arabic of the country are applied over an ointment dressing and left on 10–14 days.

Kala azar is found on the Abyssinian border; in 1935, 49 cases were admitted.

Epilepsy of unknown origin is frequent. The author postulates a parasite. *A. G. Bagshawe.*

Pervès (M.). Observations sur la pathologie du Hoggar (Tamanrasset 1933–1934). [**Observations on the Diseases of the Hoggar Country, Sahara.**]—*Arch. Inst. Pasteur d'Algérie.* 1936. June. Vol. 14. No. 2. pp. 206–220. With 4 figs. on 1 plate.

A paper on medical practice in this region, which lies within the tropic line, was summarized in this *Bulletin*, 1934, Vol. 31, p. 327.

The climate is influenced both by the Sahara and the Sudan but the dominant note is dryness, the hygrometric average being 27 per cent. The district is isolated by the desert, the nearest centres of population are some 20 days' march away, so that epidemics of short incubation are rare.

Among the nomads affections of the lungs and joints are most frequent, among the settled folk eye diseases. The pathology is

Mediterranean rather than tropical. The following are topics of interest :—

In 1933 and 1934 there were seasonal epidemics. The first was characterized by short development, three days fever and general pains followed by marked asthenia, fatality nil, nomads spared ; the second was more severe with rigors, intense headache and photophobia, and bronchitis : some old people and children died of broncho-pneumonia. Both epidemics occurred in April after the spring rains. Owing to its altitude the country is unfavourable to malaria. Sources of infection are present and several species of Anopheles. Two indigenous cases were diagnosed, unconfirmed by microscope. Venereal diseases are common, syphilis so much so as to threaten the Touareg race, especially the nomads. Among 135 cases there were noted, 4 chancres, 30 skin eruptions, 9 mucous lesions, 57 osteoarticular forms, 11 ocular syphilis, 3 congenital syphilis ; later this is stated to be general. Syphilitic affection of the joints is the rule ; of 60 cases with systems of rheumatism 57 yielded to antisyphilitic treatment ; three varieties are described. Notes and illustrations are given of six cases of juxta-articular nodules, five of which benefited from antisyphilitic treatment. The frequency of eye affections is attested by the fact that of 5,416 consultations 3,018 were for that cause—conjunctivitis of all types, trachoma (rare among the nomads), interstitial keratitis. Chronic bronchitis, in which " the rôle of syphilis is certain " is frequent. It appears that while the medical service of the stations is sufficient the nomads get little advantage from it and should be provided with a doctor who would spend his time on tour. *A. G. Bagshawe.*

GIORDANO (Mario). Uno sguardo alle attuali condizioni sanitarie dell'Eritrea. [**Review of Health Conditions in Eritrea.**]—*Rev. Parasit., Clin. y. Lab.* Habana. 1936. May–June. Vol. 2. No. 3. pp. 355–366. English summary.

Malaria is common towards the end of the rainy season, late winter and early spring, in the eastern plains, the vectors being *A. mauritianus* and *A. costalis*. Drainage and other prophylactic measures have been started and in 6 months there were 142 cases, but none fatal. Phlebotomus is present also, and three-day fever is seen. Ticks are plentiful, 22 species have been described. Here *Ornithodorus moubata* conveys relapsing fever and *Rhipicephalus simus* tick-bite fever. On some relapsing fever patients the author found lice also with spirochaetes, so that relapsing fever is both tick- and louse-borne in Eritrea. *Xenopsylla cheopis* was found, but no case of plague has been recorded. *Tunga penetrans* is said to have been imported from Somaliland a quarter of a century ago. Snakes of poisonous species are present, notably *Echis carinatus*, *Bitis arietans* and *Atractaspis irregularis* among Viperidae, and *Naia haje*, *N. nigricollis* and *N. sputans* among Colubridae. A polyvalent serum is kept. Dysentery, both amoebic and bacillary occurs, but is less frequent than formerly ; leishmaniasis and yaws are occasionally met with ; leprosy is common among the natives. *Taenia saginata* infestation is not infrequent owing to the habit of the natives of eating insufficiently cooked beef. A few cases of guinea-worm were also encountered. *H. H. S.*

Chiodi (Valfredo). Brevi cenni nosografici dell' Etiopia. [**Notes on the Diseases of Ethiopia.**]—*Giorn. Ital. di Malat. Esot. e Trop.* 1936. Aug. 31. Vol. 9. No. 8. pp. 157–160, 163. [14 refs.]

The author states that "the valorous troops of Italy having definitely obtained possession of vast tracts of Eastern Africa" a rich field of study is opened up. He divides the country into three zones: (1) The plains with gentle undulations, with an average temperature of 30°C. and a maximum of 42° in the shade. (2) Temperate levels to some 2,000 metres, with average temperature of 18°C., rarely rising to 30° and occasionally falling at night to 0°C. (3) Cold mountainous regions, about 2,400 metres, where population and vegetation are scanty.

Malaria is common; subtertian particularly, and various clinical types—dysenteric, bilious remittent, haemorrhagic and haemoglobinuric, cerebral, etc.—are seen. *Smallpox* though not often epidemic is almost constantly present, and easily spread by the nomads who live in squalor. Vaccination is not general, and is often refused. *Leprosy* is widely prevalent, nodular, anaesthetic and mutilating types being met with. *Human trypanosomiasis* is little known; *G. morsitans* and *G. palpalis* are rare, but *G. pallidipes* fairly common. Animal trypanosomiasis is better known, *T. congolense*, *T. brucei*, *T. pecorum* and *T. evansi* (particularly in camels, says the author). *Tuberculosis* is fairly widespread, and the pulmonary form runs a rapid course; surgical forms constitute about 10 per cent. of the total cases. *Relapsing fever* is "moderately diffuse," due to *Sp. duttoni* transmitted by *O. moubata*. *Venereal diseases* are a "veritable plague"; *skin affections* due to Tinea of several species also common. Parasitic infestations include hookworm, Trichuris, Ascaris and Enterobius, Schistosoma [? haematobium], Filariasis, and Dracontiasis. Several species of venomous snakes are found, notably *Echis carinatus*, *N. naja*, *psammophis* and *sepedon*. *H. H. S.*

Carrillo Gil (Alvar). Dos enfermedades por carencia en Yucatán. I. Notas clinicas sobre la xeroftalmía en Yucatán. II. Notas sobre la avitaminosis llamada "culebrilla" en Yucatán. [**Two Deficiency Diseases in Yucatán. I. Clinical Notes on Xerophthalmia. II. Culebrilla, a Form of Avitaminosis met with in Yucatán.**] —pp. 1–31. With 12 figs.; 33–58. With 10 figs. 1935. Merida, Yucatán, Mexico. [Summary appears also in *Bulletin of Hygiene*.]

I. The first of these two articles is based on a study of 109 cases seen in the Children's Hospital, Mérida. Xerophthalmia has for some years shown an increasing prevalence. Dietetic errors are doubtless at the basis of the trouble, but poverty, hunger, and intestinal diseases, in particular dysentery, play no inconsiderable part. Besides definite xerophthalmia, depicted in several striking photographs, other indications are not wanting—pallor, defective development, oedema, keratosis, ocular ulceration and staphyloma.

II. The word "culebrilla" was originally applied to any skin disease of the ringworm type, but has in more recent years come rather to be limited to an avitaminosis occurring among those living largely on maize. Some of the children affected are very wasted and cachectic, others show oedema more or less widespread, but particularly involving the legs; in some there is a purpuric eruption and local ulceration with necrosis or gangrene of the skin of the knees or elbows occurs. Which

of the vitamins is deficient to produce this is not quite certain ; some authors have ascribed it to lack of A, B and C, but others find that A, C, and D are adequate, some part of the vitamin B complex being deficient. The illustrations in this article are very descriptive. [See *Bull. of Hyg.* 1935, Vol. 10, p. 806.] *H. H. S.*

Hermans (E. H.) & Schotman (J. W.). Exotische aandoeningen in Nederland. III. Pellagra. [**Exotic Affections in Holland. III. Pellagra.**]—*Nederl. Tijdschr. v. Geneesk.* 1936. Aug. 8. Vol. 80. No. 32. pp. 3661–3669. With 6 figs. on 1 plate. English summary (7 lines).

Pellagra is, of course, by no means limited to the tropics or even warm climates, as many believe, and the interest of this case lies in the fact that from the description and the illustrations (which are exceedingly good) this was a genuine case and the first, it is said, to be reported from Holland. The patient was the wife of a sailor or boatman ; her age was 25 years, she lived in the country and came under observation on account of her mental condition—a dull state thought at first to be of an hysterical nature, but was of a schizophrenic type and did not wholly clear up. No fault, in the way of vitamin deficiency, could be discovered in her diet. The onset seemed to be in relation to the puerperium—altogether a puzzling case. *H. H. S.*

Maldonado. Champ d'action de la "Verruga" péruvienne ou maladie de Carrion. [**Verruga peruviana or Carrion's Disease.**]—*Arch. Méd. Belges.* 1936. Oct. Vol. 89. No. 10. pp. 631–658.

A general account of Verruga peruviana with greater detail of the disease in the valley of the Ste. Eulalie river. The author, who is a naturalist, describes the topographical, climatological and phytological features of the country. He notes that Verruga is most prevalent where the vegetation comprises many lactiferous shrubs and plants. Euphorbiaceae (Agaves), Julianaceae and Moraceae on the slopes ; Euphorbiaceae of other species, Papaveraceae and Asclepiadiaceae in the valley. Even after the leaves have fallen Phlebotomus find in these plants abundant sustenance while the dead leaves are nourishment for the larvae. The most heavily infected valleys are narrow, shady and tortuous, with plentiful vegetation in the first half of the year, rainfall in the first quarter, and Culex and Anopheles are abundant as well as Phlebotomus. Three species of the last occur : *P. noguchi* Shannon, a certain transmitter, *P. verrucarum* Townsend, a possible, and *P. peruensis*, a doubtful transmitter. They are nocturnal insects, biting furiously at night, hiding in the interstices of rocks in the beds of the river and watercourses and in the walls of the cultivated terraces.

H. H. S.

Kuypers (C. A.). Piedra in West Borneo.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. Sept. 15. Vol. 76. No. 37. pp. 2344–2356.

In this article abundant evidence is forthcoming of the existence of Piedra, a disease well known in Columbia and Brazil, also in West Borneo. The nodules which are characteristic of the disease are thickly set upon the terminal parts of the hair. When the hair is

stroked it feels sandy (hence the name Piedra, sand). Twenty cases were discovered among 230 Dajak men. Two forms were discovered, one with black nodules and affecting men and the other with grey-white nodules affecting mainly women, but also occasionally cultivated out of the black Piedra. Microscopically black nodules are shown to consist of a mass of large polygonal yellowish green to light brown cells with a definite cell wall. The cells of a mycelial thread are separated from one another by thick black cell walls, between which is a little intercellular light yellowish substance. By pressing on the cover glass of a caustic potash preparation the peripheral cysts are burst and the spores are set free from the nodule. Cultures can be obtained fairly pure after some two hours' treatment of the hair in absolute alcohol; the medium on which they are grown is Sabouraud's agar with the composition :—agar 25; glucose 40; peptone 10; distilled water 1,000. Incubation was at room temperature which varied from 25°C. to 35°C.

As a result of the work done in West Borneo " it appears that two Piedra forms are common, the one with black nodules in which asci with ascospores belonging to a black fungus and closely corresponding to *Trichosporon hortai*, the other with grey-white nodules caused by a grey-white fungus resembling *Trichosporon giganteum*. . . . It is almost certain that these black and white fungi are, in a botanical sense, entirely different types and cannot be included in one species."

W. F. Harvey.

Fox (Howard). **An Unproven Case of Pinta originating in Ceylon.**—*Jl. Trop. Med. & Hyg.* 1936. June 1. Vol. 39. No. 11. p. 125.

This is a short, but timely, criticism of a misleading tendency to arrive at a diagnosis of Pinta on inadequate evidence. The mere presence of coloured patches in places with depigmentation elsewhere and the cultivation of a mould, Aspergillus, are insufficient. The author states that, according to the findings of the Mexican Commission in 1929, a Wassermann positive reaction is as frequently given as in yaws or syphilis, in fact in about 98 per cent. of cases. The fungi cultivable from the skin of patients with pinta are unrelated to the disease, and the idea that different coloured pintas were due to different fungi was discarded in Mexico. The aetiological relationship of the fungi isolated to the disease is excluded for the following reasons enumerated by the author :—

" (1) In endemic regions numerous fungi (especially aspergillus and penicillium) can be cultivated from the normal skin of cases of pinta as well as from the skin of normal persons.

" (2) Cultures of fungi are usually obtained from scaly areas.

" (3) When patients with pinta change their residence to non-endemic regions the fungi usually disappear from the skin though the pigmentary changes persist.

" (4) With one doubtful exception the disease has never been reproduced in man or animal by inoculations of cultures of fungi obtained from patches of pinta.

" (5) It is difficult to understand how a superficial infection of the skin (horny layer) could cause a positive Wassermann reaction and how such an infection could be made to disappear by antisyphilitic treatment.

" (6) The occasional appearance of extensive unilateral pinta would almost preclude a local infection of the skin by fungi." *H. H. S.*

Pardo-Castello (V.). Pinta o carate en Cuba. [**Pinta in Cuba.**]—*Rev. Parasit., Clin. y Lab.* Habana. 1936. Sept.–Oct. Vol. 2. No. 5. pp. 667–675. With 7 plates. [11 refs.]

The author gives an introductory account of pinta, its history, causation, symptomatology, pathology, and treatment by bismuth and neosalvarsan. In a terminal section he considers the question of the relation of pinta to syphilis and concludes that although the pathological histology is different, there are several " points of contact " between them, notably the positive Wassermann reaction, the results of treatment by bismuth and arsenic (antisyphilitic remedies), and the frequency of cardio-vascular lesions. A history of syphilitic infection is not usually obtained and the author suggests that the relation of pinta to syphilis is similar to that between yaws and the same disease.

H. H. S.

Allen (F. R. W. K.) & Dave (M. L.). **The Treatment of Rhinosporidiosis in Man based on the Study of Sixty Cases.**—*Indian Med. Gaz.* 1936. July. Vol. 71. No. 7. pp. 376–395. With 5 figs. [91 refs.]

The authors' summary and conclusions are as follows :—

" 1. Rhinosporidium has been assigned by Ashworth to the lower fungi (*Phycomycetes*) such as the *Chytridineae* and has been provisionally placed near the *Olpidiaceae*.

" 2. In man, cattle and equines it causes an exfoliative, non-infiltrating granuloma usually situated in the nose, but also occurring in the pharynx and larynx, on the fauces and uvula, in the ear and lacrimal sac, on the conjunctiva and the mucous membrane of the glans penis and on the skin.

" 3. The occurrence of these granulomata have been reported from Asia (India, south of a line joining Bombay and Benares, Ceylon, the Philippine Islands and possibly China, Japan and the Malay States), from North America (the United States), from South America (the Argentine, Paraguay and Uruguay), from Africa (the Union of South Africa), and from Europe (Lombardy). It seems probable that the distribution is much wider than this, cases being overlooked.

" 4. The mode of infection is not known but transmission by either water or dust appears to be probable.

" 5. The authors have given reasons for believing that natural cure may sometimes take place.

" 6. Diagnosis is easy and consists of noticing the minute white sporangia on the surface of the growth and of finding the spores, containing the characteristic 10 to 16 refringent spherules, in stained smears of the secretion therefrom.

" 7. Sixty cases, investigated by the authors, are reported.

" 8. The treatment of early single growths in accessible situations is simple and consists of clean excision of the growths together with the surrounding areas of healthy mucous membrane or skin.

" 9. Treatment of the growths in inaccessible situations and of multiple growths is not so satisfactory. It consists in excision of the growths, the employment of the electric cautery for the destruction of the surrounding areas of infected mucosa and of the injection of 2 to 4 grammes of neostibosan (Bayer) in 0·3 gramme doses intravenously (adult dose) with the object of trying to kill the parasite.

" 10. The authors' cases have not been followed up for a sufficiently long period of time to enable any absolute cures to be claimed but the results reported appear to be promising.

" 11. Neostibosan is not effective in all cases and therefore a more powerful parasiticide is required, preferably one of which a single dose will prevent the development of the spores into sporangia.

" 12. Sulphostab (Boots), casbis (Bayer), entodon (Bayer), fouadin (Bayer) and paranitrophenol have been tried by the authors, and urea stibamine (Brahmachari) has been tried by Norrie in isolated cases without encouraging results.

" 13. Two patients stated that a snuff composed of pounded tobacco leaves and lime was bringing about a cure and their claim seems to be supported by the pathological report. This line of treatment, even if proved to be sure, would be very slow."

H. H. S.

Ciferri (R.), Redaelli (P.) & Scatizzi (Ida). Unità etiologica della malattia di Seeber (granuloma da *Rhinosporidium Seeberi*) accertata con lo studio di materiali originali.—Reprinted from *Boll. d. Soc. Med.-Chirurg. di Pavia.* 1936. Vol. 14. No. 5. 24 pp. With 4 figs. on 1 plate. [57 refs.]

Aiiso (M.) & Hayashi (N.). **Pathologic-Anatomical Studies of Kaschin-Beck's Disease.**—*Jl. Oriental Med.* 1936. Sept. Vol. 25. No. 3. [In Japanese pp. 467–500. With 22 figs. (2 coloured) on 8 plates. [31 refs.] English summary pp. 49–51.]

Beck's disease is defined as a condition " marked by fatigue and swelling of the phalanges ; later all the joints of the body become enlarged and normal growth is retarded." Kaschin first noted it as long ago as 1850, though it was not described in any detail till Beck gave an account of it in 1906. It appears from recent researches to be endemic from north Chosen to Manchoukuo. The authors' investigations into the pathological anatomy may be summarized thus :—

1. The most noteworthy changes are in bones and joints, but inflammation of the alimentary tract is always found.

2. The joint lesions are least in the shoulder, worst in the fingers ; swelling of joints and shortening of the bones are significant. The synovial membrane shows papillomatous proliferation, but no excess of fluid nor loose bodies are seen.

3. Synostosis of tarsal and carpal bones is not uncommon ; the joint surfaces are porous and the ends flattened. The medullary cavity is dilated (rarefied).

4. The marrow is fatty and fibrous, the latter arising from destruction of bony tissue. Deposits of iron are present.

5. The bone becomes spongy from dilatation of Haversian canals, which often contain fibrous tissue.

6. The articular cartilages show both degenerative and proliferative changes, and ulcerative processes may be seen on the articular surfaces.

7. Senile changes occur in the costal, tracheal and thyroid cartilages and blood capillaries invade the perichondral tissue.

8. The alimentary mucosa shows infiltration by lymphocytes and eosinophiles ; there may be an atrophic gastritis. The large intestine and stomach give a fairly marked reaction for iron, slight in the small intestine.

9. Iron is deposited also in the Kupffer cells and interstitial cells of the liver and in the spleen.

10. Hyaline and granular casts occur in the renal tubules, and the walls of the glomerular arteries are thickened.

11. In short the changes in bones and internal organs are of a senile character; the abundance of inorganic iron appears to be closely related, but the cause is still unknown. *H. H. S.*

Aiiso (M.) & Hayashi (N.). **The Quantity of Iron contained in the Blood in Kaschin-Beck's Disease.**—*Jl. Oriental Med.* 1936. Sept. Vol. 25. No. 3. [In Japanese pp. 513–525. English summary p. 52.]

Following up their studies on the morbid anatomy and histology of Kaschin-Beck's disease the authors have studied the iron content of the blood of these cases. In a normal man the amount is between 0·54 and 0·67 mgm. per 100 cc., with an average of 0·62. In one living in the endemic area [between Chosen and Siberia] the average is 0·58, with extremes of 0·4 and 0·69 mgm. More than two-thirds of 64 patients (45) showed a content above 0·7 mgm. One volunteer was given Ferrum redactum and his blood examined over a period of 50 days. It was observed that the blood-iron gradually increased, and then, in spite of the continued administration, gradually decreased. The authors infer that inorganic Fe plays an important rôle aetiologically. *H. H. S.*

Tessitore (C.) Un caso di *Akanthosis nigricans* presso i baboma dell' Africa Centrale. [*Acanthosis nigricans* **in a Woman of a Central African Tribe.**]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1936. Jan. Vol. 17. No. 1. pp. 49–51.

The condition, first named by Unna, is characterized by papillary hypertrophy and hyperchromia, runs a chronic course, developing in advanced age, and affecting chiefly the face, the neck, axillae, breast, elbows, flexures of the knees, and dorsa of hands and feet. The condition is rare and the case here described is the first seen by the author in 13 years' practice, 7 of them in Africa. Its aetiology is unknown; at one time it was held that there was some connexion between it and cancer for among 13 cases, 5 suffered with carcinoma of the stomach, 3 of the uterus and one of the breast. The patient whose case is related here was a woman of 60 years, belonging to the Baboma tribe; she showed the condition as affecting the eyebrows and frontal region, the neck, axillae, elbows, dorsa of hands and fingers. Her general state of health was good. No cure is known, the only effective treatment is surgical removal and this is rarely feasible on account of the extent of the lesions. *H. H. S.*

Akamatsu (A.) & Takiyama (U.). **Prevalence in Hiroshima Prefecture of Dermatitis due to the Sting of Liponyssus Nagayoi, and the Result of Studies on the Characters of that Mite.**—*Jl. Public Health Assoc. Japan.* 1936. Apr. Vol. 12. No. 4. pp. 1–2.

The authors record widespread dermatitis associated with intense itching, most prevalent during the summer months, caused by the bite of *Liponyssus nagayoi*. This mite is a common parasite of the rat; the authors have found it also on bats. *V. B. Wigglesworth.*

MEAGHER (J. L.). **Epidemic Stomatitis in the Northern Solomons causing Rapid Death.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1936. July 31. Vol. 30. No. 2. pp. 251–254.

The outbreak here recorded occurred among the natives of a small island, Matsuhan, 6 miles from Buka Passage, New Guinea. The total population was " fifteen to eighteen all told," occupying four houses near the beach. They lived by fishing, trading fish for taros. There were six fatal cases, death taking place in some within 14 hours or so, in another not till the fourth day. The chief symptoms were sore throat and mouth, vomiting (in fatal cases), dysphagia, slight cough and a remarkably red tongue. There was no complaint of abdominal pain but an early symptom in some was marked feeling of weakness with malaise. There was no fever in the cases seen by Dr. Meagher, and the pulse and blood-pressure were normal or almost normal. One on the neighbouring island of Fatsigern (she had visited Matsuhan some said on the day of the outbreak) was seen 5 days after the onset of symptoms and by that time the lips were purple, cracked and swollen, tongue " red-raw." At the junction of hard and soft palates were scattered pin-point erythematous spots, coalescing towards the uvula. No other physical signs of any import were observed [the enlarged " firm spleen reaching to the umbilicus " can have had no connexion with the acute condition].

[The author unfortunately does not seem to have seen any patients in the earliest stages, nor is there any mention of autopsy. The information is too scanty to allow of more than conjecture. Even the population of the four houses is not known for certain, and the statement that they had not eaten any fish just prior to the outbreak cannot be accepted without reserve from a village whose inhabitants lived by fishing. The symptoms are strongly suggestive of a toxin, even of a toxic food (*cf.* the fruit of *Hippomane mancinella* for instance). More detailed histories, careful post-mortem examinations and probably experimental work will be needed to clear up the mystery.] *H. H. S.*

BONNE (W. M.) & NEUHAUS (K.). Vergiftiging door de steek van een visch. [**Poisoning from the Sting of a Fish.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1936. Sept. 22. Vol. 76. No. 38. pp. 2402–2405. With 1 fig. on plate.

The fish poisoning here referred to is not from a bite but was effected through a special apparatus. On either side of the rays of the dorsal fin of *Synanceia verrucosa* are small hollow canals, which are ducts leading to poison sacs. The poison is limpid and slightly acid.

The case described is of a woman who was occupied in cleaning an aquarium and who was stung in the process by a fish. Her symptoms seem to have been extreme local pain, swelling of the punctured thumb and extension of this swelling up to the elbow, irregularity of the pulse, some cyanosis and an inclination to sleepiness. Slight incisions were made into the thumb and the wound treated with ammonia. Pain and swelling remained prominent symptoms for some days but recovery was complete. *W. F. Harvey.*

[*Synanceia verrucosa* is one of the Scorpaenidae (Scorpion Fish). Of this family there are several poisonous members. The poison apparatus, though connected with the dorsal fin, is not the same in all the varieties. Thus, in the Synanceia mentioned above, before the poison

can escape an enclosing membrane must be broken, whereas in the Scorpaena the poison apparatus is practically in direct communication with the exterior. The poison glands of both are situated at the base of the dorsal spines, but in the former the spines are grooved and a membrane makes this groove into a sac, and the poison cannot escape until the sac is ruptured, whereas in the latter the spines are channelled with an opening near the tip. Members of the Synanceia group are widely distributed.—*Ed.*]

PLUM (Preben). **Accuracy of Haematological Counting Methods.**—*Acta Med. Scandinavica.* 1936. Vol. 90. No. 4. pp. 342–364. With 12 figs. [2 pages of refs.]

This article is of fundamental importance and does not admit of abstract. Haematologists should consult the original. The author begins with an historical sketch of the development of blood-counting methods during the past hundred years and discusses their accuracy or want of it, the errors being due either to unequal distribution of the corpuscles in the counting chamber or smear, or to faulty measuring of the blood and diluent. He shows by experiment that the former of these plays the chief part in errors of individual counts, whereas the latter plays a relatively small part. The mean error in counting-chamber counts is equal to the square root of the number of cells counted; the mean error in differential count on a smear regarded as properly made may be calculated by Bernouilli's theorem $m = \sqrt{n.p.q.}$ He gives a diagram of the calculated mean error in differential counts of 100 to 1,000 leucocytes. *H. H. S.*

HYNES (M.) & MARTIN (L. C.). **A Rapid Method of measuring Erythrocyte Diameters.**—*Jl. Path. & Bact.* 1936. July. Vol. 43. No. 1. pp. 99–104. With 5 figs.

The authors describe a method of constructing a diameter distribution curve comparable to that used by Price-Jones, but performed in a much shorter time. The method consists fundamentally in the projection of the images of the erythrocytes on to a ground glass screen at 2,000 times magnification, and their direct measurement by a celluloid protractor described by Whitby and Britton in 1935. The Price-Jones method of counterstaining Romanowsky films with 5 per cent. aqueous eosin for 2 to 3 minutes is adopted. The optical system consists of a 100 candle-power Pointolite contained in a light-proof box, a lens system to condense the light on to a mirror of the microscope using a one-twelve inch oil immersion lens and a $\times 20$ eyepiece. The images of cells are transmitted from below on to the horizontal ground glass screen, extraneous sources of light being excluded by a conical black cloth. By use of this method the authors claim that the mean diameter and cell area figures may be obtained with a high degree of accuracy without pencil outlining, and that a considerable saving of time is ensured.

N. Hamilton Fairley.

COOMBS (Herbert Isaac). **Studies of the Haemoglobin and Iron of the Blood. I. The Determination of the Total Iron of Blood.**—*Biochem. Jl.* 1936. Sept. Vol. 30. No. 9. pp. 1588–1591. [11 refs.]

The author describes a method of estimating the total Fe content of the blood by the use of dipyridyl. He uses the following reagents:

(1) Fifty per cent. H_2SO_4. (2) Concentrated HNO_3. (3) Forty per cent. (approximately) sodium acetate. (4) Twenty-five per cent. (approximately) solution of glucose. (5) Dipyridyl reagent 0·468 gm. of dipyridyl in 6 ml. of N hydrochloric acid made up to 100 ml. with distilled water. (6) Standard Fe solution. 0·35 gm. ferrous ammonium sulphate in distilled water containing a few drops of H_2SO_4 and made up to 100 ml. in a standard flask. It contains 50 mgm. of iron per 100 ml.

The method is thus described :—

" Measure exactly 0·1 ml. of blood into a pyrex tube which has a mark at the 10 ml. level. The pipette should be washed carefully with the minimum of water. Add 0·2 ml. of 50 per cent. sulphuric acid and about 10 drops of concentrated nitric acid. Heat carefully, with constant agitation, over a micro-burner until charring begins. Cool and add more nitric acid, repeating these operations until no further charring occurs. Boil off the excess of nitric acid. The residual drop of sulphuric acid usually contains a white precipitate which is probably anhydrous ferric sulphate. Add about 0·5 ml. of water and warm to dissolve this precipitate. Add 0·3 ml. of dipyridyl reagent, followed by 1 ml. of glucose solution. Mix well by shaking and add 5 ml. of sodium acetate solution. Heat in a boiling water bath for 5 min. for full colour development. Cool and make up to the 10 ml. mark with distilled water.

" The standard is prepared in exactly the same way except that 0·1 ml. of the standard iron solution (or 1 ml. of a standard diluted ten times) is used in place of the blood.

" Compare in a colorimeter with the standard preferably at 25 mm. If *U* is the reading for the unknown and *S* the reading for the standard, then $\frac{S \times 50}{U}$ = mg. of iron per 100 ml. of blood."

Normally, human blood contains about 50 mgm. of iron per 100 ml., and 0·1 ml. is enough for making the estimation, unless there is marked anaemia when this volume should be doubled.

The author has carried out some hundreds of analyses and has checked his findings in many ways ; he finds this dipyridyl method very reliable. *H. H. S.*

Symons (P. H.). **A Colour Index Calculator.**—*South African Jl. Med. Sci.* 1936. June. Vol. 1. No. 4. pp. 172–175. With 3 figs.

The author states that the instrument depicted in this paper has been devised and constructed because " the calculation of the large number of colour indices required in haematological practice is apt to prove exceedingly tedious." For his calculations he takes the fundamental equation $\frac{H}{100} \times \frac{S}{E} = C.I.$, where H is the haemoglobin percentage, S the erythrocyte standard in millions per cmm., E the estimated erythrocyte number in millions per cmm. in the case in question, and C.I. the colour index. He states that a scale based on common logarithms would be more satisfactory, the equation becoming $\log H + \log S - \log E - 2 = \log C.I.$

A circular rotating scale graduated on this basis proved satisfactory on trial ; next a cylindrical projection was also used with success, but these earlier instruments have now been simplified to a slide rule form clearly shown in an illustration.

[It all seems very simple, so simple in fact that the reviewer feels that he must have overlooked something, but if the erythrocyte standard is

accepted as 5 million per cmm., as the author does (though this is by no means generally held nowadays) and if the haemoglobin is registered as a percentage of a somewhat arbitrary standard (and this has been replaced by the more accurate "grams per cent."), then the simple calculation of $\frac{H}{2E}$ (E being the first two figures of the estimated erythrocyte count) gives the C.I. as rapidly as the more elaborate logarithm and slide rule method.] *H. H. S.*

ANDRESEN (Marjory I.) & MUGRAGE (Edward R.). **Red Blood Cell Values for Normal Men and Women.**—*Arch. Intern. Med.* 1936. July. Vol. 58. No. 1. pp. 136–146. With 2 charts. [22 refs.]

The subjects of this investigation were 40 white men and 40 white women, between 20 and 45 years of age, who had been living in the district [? Denver; the place is said to be 5,000 feet above sea-level and the authors are Denver physicians, but the place of the investigation is nowhere mentioned] for at least two years; the number included physicians, medical students, technicians and office workers. The various findings are given in protocols; the results only can be indicated here :—

In all 240 samples of blood were examined as regards the number of erythrocytes, the volume of packed cells and the haemoglobin amount. The last was made in three ways, *viz.*, the Van Slyke-Neill manometric gas analysis to determine the oxygen-carrying capacity; the iron content of the whole blood, and estimation after conversion to acid haematin and the content of the Hb in grams calculated. The three methods yielded closely comparable results. The mean Hb value for the men was 16·54 gm. and 14·45 gm. for women per 100 cc. The mean packed cell volume per 100 cc. was 48·35 cc. and 43·22 cc. respectively, and the mean erythrocyte counts 5,420,000 per cmm. for men and 4,630,000 for women. The mean corpuscular Hb. value was 30·5 micromicrogram for men, 31·2 for women (Wintrobe's figures were 29·2 and 28·8 respectively) and the mean corpuscular volume, 89·2 cubic microns for men and 93·3 for women, was also above Wintrobe's average (86·5 and 87·0). The mean corpuscular haemoglobin concentration was 34·2 per cent. for men (Wintrobe gives 33·7) and 33·4 for women (Wintrobe gives the same)—evidence of the constant value of this is normal blood. Additional interest is obtained from a perusal of the author's findings because nearly all previous results have been recorded in those living at, or not more than 1,000 ft. above, sea level.

H. H. S.

HENNESSEY (R. S. F.). **Haematological Observations on Natives of Uganda.**—*East African Med. Jl.* 1936. Oct. Vol. 13. No. 7. pp. 210–215.

This haematological study was undertaken with a view to determining the standards for the normal healthy native in Uganda; the subjects were adult male convicts believed to be physically fit. The red corpuscle counts ranged between 3·5 and 6·25 millions, the mean being 4·56 per cmm., a figure some 17 per cent. below Price-Jones's figure (5·5) for Europeans. Haemoglobin was estimated by a Sahli instrument corrected by a new Hellige haemometer; the percentage ranged

between 70 and 115, with a mean of 95, an equivalent of 13·1 gm. per cent. The usually accepted European figures are a range of 12·4 to 17·0 gm., with a mean of 14·7. Here again, it will be seen, the native standard is below the European. The corpuscle diameter is greater, between 7·4 and 8·8 μ, with a mean of 7·88, the European mean being 7·17 μ. Less reliance is to be placed on leucocyte counts for the chances of small unrecognized infections are so great in the tropics. The author found the total to range between 5,400 and 12,600 per cmm. with a mean of 8,104. The European mean of Price-Jones is 8,007 with extremes of 2,002 and 14,013 (these were regarded as healthy subjects). The author suggests that the circulating haemoglobin of Uganda natives may be maintained at an efficient level by erythrocytes, fewer in total but larger individually, than those of Europeans. *H. H. S.*

DE MELLO (Froilano). Sur la genèse des altérations rencontrées dans le sang d'individus apparemment normaux de l'Inde Portugaise. [**Blood Changes in Apparently Normal Inhabitants of Portuguese India.**]—Reprinted from *Medicina.* 1934. Nov. 13 pp.

The author has recorded certain findings in the blood of 60 individuals in Portuguese India to all outward appearance healthy. He studied the total erythrocyte and leucocyte counts, a differential count of the latter, the haemoglobin percentage by the Gowers-Sahli apparatus, in three groups of 20 each, aged 7–14, 14–20 and 20–45 years. In the first the red cell counts ranged between 4,100,000 and 7,680,000 ; in the second between 5,000,000 and 8,400,000 ; in the third between 4,960,000 and 7,360,000, and the corresponding white cell limits 4,100 and 8,400 ; 4,100 and 9,800, and 4,100 and 8,300. In none of those below 14 years was the haemoglobin 100 per cent., the limits were 80 and 98, in the second group 72 and 100 and the third 74 and 100. An eosinophilia of 8 per cent. and over was found in 11 of those under 14 years, in 6 of the second group and 3 of the third. Relative lymphocytosis was present in all but three of the total, two in group 2, one in the third group. The author is of opinion that the eosinophilia is helminthic in origin and the lymphocytosis the result of latent malaria.

H. H. S.

NAPIER (L. Everard). **Tropical Macrocytic Anaemia.**—*Lancet.* 1936. Sept. 19. pp. 679–683. With 3 figs.

The author points out that the term tropical macrocytic (or megalocytic) anaemia, introduced by Dr. Lucy WILLS, has found its way into text-books without any very exact definition of either the clinical syndrome or the haematological picture that it represents. WILLS regarded the condition as a dietetic deficiency and distinguished it clinically from pernicious anaemia by the absence of both natural remissions and neurological features. The presence of free acid in the gastric secretion, the absence of hyperbilirubinaemia and of urobilinuria, the leucocytosis, the inversion of the polymorphonuclear-leucocyte rates and the absence of any right-hand shift in the Arneth count further differentiated the two diseases. The deficiency factor in the food of such patients was supplied by marmite or liver extract and appeared identical with Castle's extrinsic factor.

Excluding three cases of pernicious anaemia and two cases with sprue-like conditions, there were eleven cases of macrocytic anaemia in

the author's series which responded to treatment with marmite. Of these four were non-pregnant women and seven were men. The symptoms that brought the patients to hospital were referable to anaemia, *i.e.*, weakness, lassitude, shortness of breath and exhaustion on exertion. Nervous features were absent. A history of irregular fever was given by four patients with an enlarged spleen, but in no case was fever prominent. Malaria and kala azar were excluded. The haematological findings were similar to WILLS's tropical macrocytic anaemia except that the indirect van den Bergh reaction was positive in nine out of the eleven cases, the quantity varying from 1 to 3 units. There was other evidence of blood destruction including reticulocytosis which was most marked in cases with splenomegaly. The alcohol test meal showed hypoacidity in three, normal acidity in four and hyperacidity in two patients.

The reticulocyte response to marmite was inadequate, even in those more severely anaemic, though its therapeutic effects were striking. The author suggests that the submaximal reticulocytosis may have been due to inadequate dosage, while the action of marmite itself was attributed to its containing an independent haemopoietic principle which was also present in liver and probably other food substances as well. The cases, however, did not constitute a homogeneous group. One group in which there was evidence of dietary deficiency corresponded closely to WILLS's tropical macrocytic anaemia, whereas in the second group associated with splenomegaly, fever and reticulocytosis some haemolytic process appeared to be operative which brought about a relative deficiency in the specific haemopoietic (marmite) principle in people who are on a diet low though not actually deficient in this factor. It was suggested that the term "Bengal splenomegaly" might be applied to this group.

[An example of the disease now described by Napier under the title "Bengal splenomegaly" was recorded by the reviewer 2 years ago (*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934, XXVII, (563) under the heading "Rarer Forms of Megalocytic Anaemias encountered in Tropical Practice." This patient had never been further east of the Indian mainland than Delhi; he had spent several periods ashore in Bombay and once he had called at Calcutta, but had not left the ship. Whilst there are justifiable grounds for regarding the disease as a new entity, the term "Bengal splenomegaly" appears hardly appropriate on geographical grounds since the first case was described from the Punjab.] *N. Hamilton Fairley.*

DHAR (Jyoti). **Haematological Studies in Indian Women. (Part Five.) A Preliminary Report on the Determination of the Normal Reticulocyte Value in Eighty-Six Healthy Bengali Women.**—*Calcutta Med. Jl.* 1936. Sept. Vol. 31. No. 3. pp. 132–154. [37 refs.]

The greater part of this article is devoted to a general account of the reticulocyte, of the literature on the subject, the structure and characteristics of the cells. The author's study is based on the percentages in 86 non-pregnant, to all appearances healthy, Bengali women between 16 and 35 years of age. No selection was made with reference to menstruation. He found that amongst his 86 subjects the average count was 0·945 per cent. of red cells, the highest count being 2 and the lowest 0·3 per cent. A very large proportion, 93 per cent., ranged between 0·3 and 1·4, which he consequently regards as the normal range

for Indian women. His average counts were considerably above those reported by other workers whose methods he deems less reliable than that employed by him, the method recommended by the American Society of Clinical Pathologists, using saturated alcoholic solution of brilliant cresyl blue and 1 per cent. neutral potassium oxalate in 0·85 per cent. sodium chloride solution. *H. H. S.*

Wells (L. H.). **Diurnal Fluctuations of the Leucocyte Count in Man.**—*South African Jl. Med. Sci.* 1936. June. Vol. 1. No. 4. pp. 157–168. With 3 figs.

This will prove a very useful paper if it merely drives home the fact that very little information of value can as a rule be deduced from a single leucocyte count made at any time in the 24 hours. Fluctuations in normal subjects are great and change may take place within a brief interval.

The author's observations were carried out on young male adults, 22 series being obtained, and examinations being made when possible every fifteen minutes. Personal errors may have had something to do with the variations, but these are altogether too great to be thus accounted for. The detailed results are given in a table. The lowest count was 5,600 ; the majority were between 7,000 and 8,000 (9), next between 6,000 and 7,000 (7), two were below 6,000 and four above 8,000. The highest ranged between 10,600 and 22,100. In one subject there was a rise from 9,200 to 14,800 in half an hour ; in another from 9,600 to 15,300 in three-quarters of an hour and in a third an even greater change, 5,900 to 18,500 in the same time.

There was clear evidence of a usual leucocytic tide with an ebb in the early morning and a flow in the early afternoon, but there were minor fluctuations of irregular occurrence. It was found that the fluctuations of the total leucocyte count did not follow those of the neutrophile count ; the differential counts in this series, however, are not discussed in detail.

Stammers, who has also studied the question, ascribed the modification of the differential count to increased ultra-violet radiation, not to altitude alone, but to the combined effect of altitude and climatic factors. But Bantu subjects gave results closely similar to those of Europeans, and if the pigmented skin of the former is, as is believed, an efficient screen against U.V. radiation, the cause for the change in the leucocyte count must be looked for elsewhere. *H. H. S.*

Kennedy (Walter P.) & Mackay (Ian). **The Normal Leucocyte Picture in a Hot Climate.**—*Jl. Physiology.* 1936. Sept. 8. Vol. 87. No. 4. pp. 336–344. With 2 figs. [13 refs.]

Continuing their work on blood conditions in hot climates [see this *Bulletin*, 1935, Vol. 32, p. 528 ; 1936, Vol. 33, p. 480] the authors have investigated the leucocytic picture of 177 airmen and officers of the R.A.F. stationed at Hinaidi, men who had been in Iraq for at least a year and had good health records. For comparison they examined the blood of 32 airmen in Transjordania, 33 in Aden, 29 in Khartoum, and 29 'Iraqi medical students from Baghdad. Altogether, therefore, there were 271 British airmen and 29 'Iraqui students, under subtropical conditions.

They found that " neutrophils were relatively reduced, the monocytes increased, as compared with British standards. The polynuclear

count was deviated to the left. An unusually high number of 'abnormal' cells was found." Abnormal include cells promyelocytes, eosinophil myelocytes, macropolycytes, lymphoblasts and Türk cells and also erythroblasts. After consideration of possible factors, the authors conclude that the changes are probably due to climate.

H. H. S.

SHAW (A. F. Bernard). **The Polynuclear Count in Egyptians and British Subjects Resident in Egypt.**—*Jl. Path. & Bact.* 1936. July. Vol. 43. No. 1. pp. 165–172. [14 refs.]

Following the introduction of the polymorphonuclear count or Cooke and Ponder's modification of the Arneth count, recent researches have confirmed the work of earlier observers and shown that locality may have a decided influence in producing a left-handed deflection in the population compared to the European standard. In the present investigation blood films were fixed in methyl alcohol for 10 minutes and then stained with Giemsa 1·0 cc. in 10 cc. of distilled water for 20 minutes. The criteria of Cooke and Ponder for nuclear lobulation were strictly adhered to. Samples were collected between 9 a.m. and 10 p.m. A differential count of 500 cells was done in each case, but total leucocyte counts were not made. The Egyptian and British residents in Egypt both showed a marked left-handed deviation characterized by a relative excess of cells in classes I and II, and a relative deficiency in classes III, IV and V. Compared with KENNEDY's results for Britain these results proved statistically significant. There was, however, no significant difference between the Egyptians and the British domiciled in Egypt. Similar results have been obtained by KENNEDY and MACKAY amongst British airmen stationed in Iraq and the indigenous population. The fact that the count of British subjects domiciled in Egypt and Iraq conforms with that of the inhabitants of these countries, while differing from the count in Great Britain, indicates that the condition is environmental and not racial in origin. British subjects from Egypt within a few weeks assume the British type of count on arrival in England, but revert to the Egyptian type on returning to Egypt. [See also this *Bulletin*, 1936, Vol. 33, pp. 480, 803.]

N. Hamilton Fairley.

SALAH (M.). **Studies on Anaemias in Egypt. V. Acholuric Jaundice.**—*Jl. Egyptian Med. Assoc.* 1936. May. Vol. 19. No. 5. pp. 205–228. With 4 figs. on 1 plate.

The author describes three cases of familial acholuric jaundice in a mother and two daughters, and two cases of acquired acholuric jaundice. The familial group had all showed a tendency to haemorrhage since childhood. The first two patients were typical inasmuch as there was splenomegaly, anaemia, jaundice, increased fragility of corpuscles, marked microcytosis, high reticulocyte counts, high icterus index and urobilinuria. The third did not present the manifestations of the active phase of the disease but the haematological findings were characteristic. The author raises the question whether the association of acholuric jaundice and haemorrhagic diathesis in this family indicates a combined constitutional abnormality of both erythrocytes and platelets, or whether it suggests a constitutional hypersplenism leading to haemolysis and intermittently excessive

destruction of platelets. The low platelet counts in the first two patients manifesting evidence of haemolysis suggests the latter interpretation. Splenectomy without blood transfusion was performed in the first two patients with satisfactory results. The jaundice disappeared by the end of the first week, and the reticulocyte count became normal three to four days after operation. Haemoglobin improved and the diameter index showed a slow increase which started about the end of the first week. In contradistinction to the findings in thrombocytopenic purpura, though the platelet counts improved, the tendency to haemorrhage remained.

In the two cases of chronic haemolytic anaemia classified as acquired acholuric jaundice of Widal-Hayems there was no increased fragility, no microcytosis and no family history. They resembled Cooley's type of erythroblastic anaemia as regards age, type of anaemia and splenomegaly, but the type of nucleated red cells were normoblasts, the erythroblast of the type met with in Cooley's anaemia being found only twice in Case I. The absence of changes in the short and long bones of the skull was regarded as the only point differentiating them from typical Cooley's anaemia of a similar age. *N. Hamilton Fairley.*

BLACKIE (W. K.). **The Anaemia Problem in Southern Rhodesia.**—*South African Med. Jl.* 1936. June 13. Vol. 10. No. 11. pp. 393–398.

In Southern Rhodesia disease, climate, diet and altitude play an aetiological rôle in anaemia which contributes to a subnormal state of health.

The diseases more directly concerned are malaria, blackwater fever and bilharzia. Malaria is almost entirely due to *P. falciparum* and the strains met with in Southern Rhodesia are capable of causing, either directly or indirectly, more severe degrees of chronic anaemia than those recently recorded by FAIRLEY and BROMFIELD in their London series. Chronic malarial gastritis may also predispose to anaemia. In blackwater fever sudden severe haemolytic anaemia is characteristic, and since routine blood transfusion has been adopted at the Salisbury Hospital the number of patients dying from anaemia has fallen to vanishing point. Bilharzia disease, though more insidious, is capable of giving rise to moderate degrees of anaemia—especially amongst children. *S. haematobium* is more common than *S. mansoni*, though both species are prevalent.

During the heat of the summer months free perspiration occurs and this has been shown to have a remarkably high chloride content. The blood chlorides tend to fall with reduction in the secretion of hydrochloric acid and consequent defective absorption of iron. The altitude is about 5,000 feet, but in assessing anaemic states no special allowance need be made for this.

Diet is important. A considerable proportion of Europeans—especially females—subsists on a diet containing minimal amounts of iron. Amongst Europeans the protein moiety of the diet is adequate to supply extrinsic factor, but instances of tropical macrocytic anaemia are occasionally encountered amongst the native races and are explicable on this basis ; the disease responds adequately to liver extract and marmite.

Nutritional anaemia is by far the commonest type encountered ; it is frequent in females of any age. Only three cases of idiopathic

hypochromic anaemia were met with and one of these presented a characteristic Plummer-Vinson syndrome.

The author concludes by urging a full haematological examination in medical, surgical and gynaecological cases in a country where anaemic states arise with such insidiousness. *N. Hamilton Fairley.*

CRANDALL (Noble F.). **Hemophilia in the Negro.**—*Trans. College of Physicians of Philadelphia.* 1936. 4th Ser. Vol. 4. No. 1. pp. 57–58.

The author has made a careful study of medical literature but has not discovered any account of haemophilia occurring in a negro. Hence, in that here recorded there is absence of the usual family history of " the hereditary tendency of males to bleed." The patient gave a history of excessive haemorrhages since early childhood [the age of the patient is not stated]. He developed hemarthrosis of the left knee. Coagulation time was tested on 13 occasions and was found abnormal on twelve. Five months after the bleeding stopped the coagulation time was still much prolonged. " The platelet count, the tourniquet test, the clot retraction, the Wassermann and Kahn tests were all negative," states the author [but he does not define what he implies by a " negative platelet count " ; as a rule the platelet count is normal]. *H. H. S.*

Report upon Mosquito Control Activities, 1935, the Des Plaines Valley Mosquito Abatement District.—40 pp. [Summary taken from *Public Health Engineering Abstr.* Wash. 1936. Nov. 7. Vol. 16. Signed E. M. WATKINS.]

Mosquito annoyance during 1935 was the highest since the beginning of operations in 1928 in spite of the most complete control of breeding. Cloud-bursts caused larvae and pupae to go down the Salt Creek into the district, breeding then beginning in the flooded bottom lands. This is the first definite record of the river as a distributor of *Aëdes vexans* larvae, and shows the necessity of keeping a close watch for the recurrence of conditions that would wash larvae or pupae into the river from back pools. During the middle of August the district received the worst flight of *Aëdes vexans* it ever experienced. Prior to this flight, during the month of August, no rain of any consequence had fallen within the district. As all breeding areas were then under control and local breeding having been ruled out, it gave the assurance that the presence of mosquitoes was not the result of local breeding. Following this flight, four other major flights took place, two from the south and two from the west, which indicated that tremendous numbers of larvae had been breeding in the marshes to the west and south of the controlled area. The extensive drainage which has taken place in Stickney Township during the past few years and its effectiveness in withholding breeding in this area is the one indication that flight centers may be broken up. With the progress in drainage and the increased efficiency in oiling, the problem of mosquito flight becomes more in evidence and the eventual mosquito-proofing of the controlled district apparently depends upon the ability to stop the long flights from the west and the south.

Progress was carried on in temporary control operations during 1935 with relief labour forces, through the Illinois Emergency Relief Commission up to August 15th and with forces supplied by WPA after

that date. Figures are given showing work accomplished, together with a cost distribution summary of previous years and a more complete analysis for 1935.

The finding of *Anopheles punctipennis* in large numbers indicated control measures should be taken against this species, and Paris green dusting was inaugurated with gratifying success. Discovery of *Culex territans* and *Culex pipiens* as the two principal species breeding on home premises was also noted.

Using the year 1928 as a basis of comparison with 1935 in regard to general meteorological conditions, it was found that in comparing the fauna with 1935 the outstanding factor has been the reduction in numbers of the domestic type of mosquitoes and the practical extinction of the woodland group. The marsh mosquitoes on the other hand have not shown a corresponding decrease in numbers, indicating that control of this species under excessive breeding conditions has not been accomplished. Its long flight range habits, as well as the tremendous reproductive capacities which it has shown, indicate that the problem is one which only further study and application can solve.

Salient drainage feature of 1935 was the particular emphasis placed upon wet lot drainage flooded by spring rains, and with completion of control measures as planned for 1936, it is expected that perfect control will result within the boundaries of the district even in the event of excessive rains as were experienced during 1935.

By use of charts, the flight of the marsh mosquitoes *Aëdes vexans* into the Des Plaines Valley Mosquito Abatement District over a period of eight years is shown, proving that the year 1935 far surpassed any previous year in this regard. By means of these charts it is hoped to learn the location and exact character of the large breeding areas, in order that control methods be made to make the district mosquito-proof.

GORE (Ramkrishna N.). **A Village Mosquito-Trap.**—*Indian Med. Gaz.* 1936. Aug. Vol. 71. No. 8. pp. 460–461. With 4 figs.

The author describes a simple but ingenious trap with which it may be possible to reduce the number of adult mosquitoes in rooms. It consists of a large clay pot of a type common in the village, provided with a piece of cloth hanging so as to form a sleeve inside the pot, thus rendering it more attractive. It is suggested that if the contents of the room are disturbed in the morning, an increased number of mosquitoes will find their way into the trap, and that they can be killed by placing it in the sun or in other ways. On one occasion the author has killed as many as 245 mosquitoes with one of these traps, but he gives no details about the sex of the mosquitoes or of the species to which they belonged. *P. A. Buxton.*

GALLIARD (H.). L'anthropophilie de *Culex fatigans* au Tonkin. [**Anthropophily of** *Culex fatigans* **in Tonking.**]—*Bull. Soc. Path. Exot.* 1936. May 13. Vol. 29. No. 5. pp. 517–518.

The author points out that in some places in the tropics *Culex fatigans* bites man, in others it does not. [He might have added that in Calcutta it is common at nearly all times of year, though it only becomes a serious nuisance to man for a short period each year. See Senior WHITE, *Bull. Entom. Res.*, 1934, Vol. 25, p. 551.] The author

holds that some of the differences in this respect are due rather to the imperfection of experiments than to any real difference in the avidity of the mosquito for human blood. *P. A. B.*

Fink (David E.) & Haller (H. L.). **Relative Toxicity of Some Optically Active and Inactive Rotenone Derivatives to Culicine Mosquito Larvae.**—*Jl. Econom. Entom.* 1936. June. Vol. 29. No. 3. pp. 594–598. With 1 fig.

The authors study the toxicity of certain compounds derived from the plant *Derris*: their insecticidal value is determined upon batches of larvae of *Culex*.

It is generally known that powdered *Derris* root contains insecticidal substances which are of great potential value though not very regular in their effect. It is generally held that rotenone is the most strongly insecticidal among the substances which have been isolated and studied. Several new compounds closely similar to rotenone in molecular structure have been isolated. The present paper describes the result of testing them, in very fine suspension in water, against *Culex* larvae. It is clear that, over a wide range of concentrations, optically active dihydrodeguelin and rotenone are much more insecticidal than four other compounds which were tested.

It is not likely that rotenone insecticides will be of much value against mosquito larvae, because of the cost of dealing with large volumes of water. But the work is of great interest because it points to ways in which insecticides derived from *Derris* might be made more sure and efficacious in their effect on fleas and many other insects. *P. A. B.*

Gibbins (E. G.). **Uganda Simuliidae.**—Reprinted from *Trans. Roy. Entom. Soc. London.* 1936. June 19. Vol. 85. Pt. 9. pp. 217–242. With 24 figs.

In this paper the author adds to the information which he has already published on the systematics and biology of species of *Simulium* occurring in Uganda.

The part of the paper of most interest to readers of this *Bulletin* is that which deals with *Simulium damnosum*. The author refers to the medical importance of this insect as a host of *Onchocerca volvulus*, which is now known to be associated in the Congo and the Sudan with blindness. It appears that in Uganda the adults of this insect are capable of flying great distances and in sufficient numbers to cause annoyance. They have twice raided Kampala, though local investigations appear to have shown that there are no breeding places nearer than the Nile, 45 miles away.

The great part of the paper is systematic and deals with nine species of which five are described as new. The author gives descriptions in nearly every case of the male, female, early stages and breeding place. The paper is fully illustrated. *P. A. B.*

Tonnoir (A. L.). Notes synonymiques sur quelques *Psychodidae* (Diptera). [**Note on Psychodidae.**]—Reprinted from *Bull. et Ann. Soc. Entom. de Belgique.* 1934. Vol. 74. pp. 69–82. [26 refs.]

Only a small part of this paper is of interest to the readers of this *Bulletin*. In 1915 Taylor described a Psychodid from Queensland as

Pericoma townsvillensis, and stated that it " is a very severe biter, the irritation remaining for some hours." This has stood as the only record of a Psychodid (other than *Phlebotomus*) sucking blood.

The author of the present paper, in the course of a general revision of the family, has examined some of the original material. In his view it is referable to the genus *Telmatoscopus* ; dissection clearly shows that the insects could not have sucked blood. *P. A. B.*

Quarterly Bulletin of the Health Organisation. League of Nations. Geneva. 1936. June. Vol. 5. No. 2. pp. 211–236. With 4 figs.—**The Fly Problem in Rural Hygiene. I. Report of the Meeting of Entomologists convened by the Health Organisation of the League of Nations on the Fly Problem in Rural Hygiene, held in London on December 16th and 17th, 1935. II. The Biothermic Method of Fly Destruction and the Ease with which it can be adapted to Rural Conditions** [Roubaud (E.)]. **III. Investigations into the Fly Density in Hungary in the Years 1934 and 1935** [Lörincz (Francis) & Makara (George)]. **IV. On Flies visiting Human Faeces in Hungary** [Lörincz (F.), Szappanos (G.) & Makara (G.)].

The series of papers, the titles of which are given above, relate to conditions in France and (more especially) Hungary, and are consequently of only indirect tropical application, if any. Nevertheless, it is to be observed that the " Report," while noting that " The fly problem in Eastern countries appears to differ in many respects from that in Europe," recommends that the matter " should form a subject for discussion at the Conference on Rural Hygiene for Eastern Countries in 1937." As regards the biothermic method for the prevention of fly-breeding in stable-manure (II), Roubaud claims that " At the Pasteur Institute of Nha Trang [French Indo-China], pits with sliding cob covers resting on the manure are used with great success." In Hungary it appears (III) that " house-flies do not breed in human faeces," and that " neither village latrines nor human faeces exposed in the open are as frequently visited by house-flies as has been previously supposed." [To what extent, if at all, racial differentiation plays a part in the local importance of *Musca domestica* as a disseminator of intestinal disease has yet to be proved.]

E. E. Austen.

Ford (Norma). **Further Observations on the Behaviour of *Wohlfahrtia vigil* (Walk.) with Notes on the Collecting and Rearing of the Flies.**—*Jl. Parasitology*. 1936. Aug. Vol. 22. No. 4. pp. 309–328. With 4 figs. & 1 map. [22 refs.]

The author has added considerably to what is known of the habits of *Wohlfahrtia vigil* and observed a number of cases of myiasis due to infestation by its maggots in Canada.

It appears that myiasis due to *Wohlfahrtia vigil* is much commoner than had been supposed : from cases in infants who were observed in June, 1934, in Toronto, Canada, it is clear that the larvae in their first stage are capable of penetrating healthy skin, and that extensive damage frequently results. They are a definite danger to infants sleeping out of doors, but it seems that they cannot penetrate the skin of an adult human being.

The adult fly does not visit carrion and is not commonly attracted to flowers, though there are circumstances under which individuals of both sexes can be taken on flowers of particular sorts.

The female appears to be more active at dusk, and capable of entering the hole of an animal and discovering its host in partial darkness. This has been actually observed in the laboratory, young mice being exposed in a box in a cage containing flies. In general the female deposits living larvae, but occasionally eggs are also produced; in this event they hatch almost at once. It appears that the larvae can go through the whole period of growth in four days in a living mouse. If it is removed partly grown from its host it is capable of feeding on meat and completing its growth. *P. A. B.*

Canavan (W. P. N.). **Occurrence of Intestinal and Nasal Myiasis in Oklahoma.**—*Jl. Parasitology.* 1936. Apr. Vol. 22. No. 2. pp. 228–229.

Reference is made to a previous publication by Meleney and Harwood of a case of intestinal myiasis with the larvae of *Hermetia illucens*, the soldier fly, and three more cases of myiasis are briefly noted, all occurring in Oklahoma City. The first was a boy of 6 years, suffering from fever of 104°F., abdominal pain, vomiting and diarrhoea, whose symptoms cleared up immediately after passage of the larvae. The second was a girl of 12 years, working on a farm, who in a fit of convulsions coughed up 2 larvae and 56 pupae of *Stomoxys calcitrans*. The third was also a young girl [age not given] from whose nose were extracted 26 larvae and 13 pupae of the Texas screw-worm fly, *Cochliomyia hominivorax*. *H. H. S.*

Mariani (Giacomo) & Besta (Bruno). La blatta orientale serbatoio di protozoi ed elminti. [**The Cockroach as a Reservoir of Protozoa and Helminths.**]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1936. Mar. Vol. 17. No. 3. pp. 177–184. [19 refs.]

The author examined 93 cockroaches, *Periplaneta orientalis*, captured in the hospital, the street, the Lazaretto, the laboratory of Mogadiscio, Somaliland, and found in their alimentary canals, flagellates, Trichomonas and Chilomastix, amoebae, infusoria, spirilla, and helminth ova, Enterobius, Trichuris, Ascaris, and Blastocystis. When allowed to feed on bread inpregnated with faecal matter containing *E. histolytica, E. coli, E. nana*, flagellates and Blastocystis, the cockroaches were found to retain them alive for 1 to 20 days and this insect may, therefore, act as a transmitter of infection. *H. H. S.*

Latychev (N.). Expérience d'application de certains dérivés de benzol dans la lutte contre les tiques *Ornithodorus papillipes*. Communication préliminaire. [**Benzol Derivatives for Eradication of Ticks.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1936. Vol. 5. No. 2. [In Russian pp. 174–178. French summary p. 178.]

Ticks, especially *Ornithodorus papillipes*, carrying pathogenic spirochaetes in Central Asia may transfer infection to their offspring and their nests may retain the infection for years; hence the importance of destroying and getting rid of ticks. Hydrocyanic acid has proved

totally inadequate, even in high concentration ; chloropicrin is better but after its use it hangs about the dwelling and is got rid of with difficulty. The author has carried out laboratory experiments with benzol preparations, notably paradichlorobenzol, and reports that the results are very promising. *H. H. S.*

Chopra (R. N.). **Control of Drugs in India.**—*Bombay Med. Jl.* 1935. Nov. Vol. 4. No. 11. pp. 219–222. Also in *Jl. Indian Med. Assoc.* 1935. Dec. Vol. 5. No. 3. pp. 121–125.

Bombay Medical Journal. 1935. Dec. Vol. 4. No. 12. p. 242. —**A Pure Drugs Act for India.**

The *Indian Medical Gazette* has described India as " a land of quacks, quack traders, and quack medicines." Drugs and chemicals of defective strength and impure quality pour into India and untested sera and vaccines are freely sold. Druggists are unqualified.

Some years ago a small committee, of which the author was chairman, was appointed to study the question. It reported in 1930, but owing to " financial stringency " no Government action has been taken. The subject is here discussed with reference to the drugs and chemicals of the British Pharmacopoeia, those known as approved medicines and the group of patent and proprietary medicines. It is stated that firms abroad manufacture drugs specially for the Indian market and are able to undersell the local manufacturers, who consequently lower the quality of their own products.

The Drugs Enquiry Committee collected samples at random from different Provinces, which the author analysed. Adulteration was common and many packages were under strength as well as under-weight. In some instances quinine tablets contained no quinine. Biological products and organic compounds containing arsenic and antimony may be satisfactory when imported but climatic conditions and defective storage produce rapid deterioration, and many retail sellers have no proper storage arrangements. The practice actually obtains of buying up time-expired products in Europe and loosing them on India at a cheap rate. Many of the Indian products moreover are not up to standard and they are put on the market with toxicity and strength untested. Of the patent and proprietary medicines it is unnecessary to speak ; the Indian public consumes them " voraciously."

The author points out such dangers as the use of anti-diphtheritic serum of uncertain strength and of faked insulin in diabetic coma as well as the risk to life of impure organo-metallic compounds.

At present mere adulteration of drugs is not prohibited in India by enactment, nor is the sale of a drug below standard punishable except on the basis of misrepresentation or fraud. What is required is central as well as provincial legislation, machinery to test medicinal preparations and inspectors to collect samples. There are, however, difficulties : *e.g.*, the profession of pharmacy is unorganized in India ; " anyone can compound and sell medicines," and the drugs used in the indigenous systems of medicine, largely employed, cannot be brought into any scheme for there are no standards. The following resolution passed by the Sind Medical Union aptly sums up the situation—

" The Sind Medical Union notes with regret and concern the Government of India's deliberate apathy to standardise and control the purity and strength of drugs and medicinal preparations, and to penalise adulteration

thereof, by an Act of legislature, the great importance and necessity for which has been fully shown by the Chopra Committee Report in 1930. The Union urges the Government to enact a law at the earliest sessions of the Assembly, as the welfare of the public is being constantly jeopardised more and more by an increasing number of spurious drugs and biological products imported from foreign countries which has also induced some local manufacturers to produce non-genuine drugs and preparations to compete with the cheaper foreign stuff or otherwise to exploit the local market.

"The Union further urges the Government to enact concomitantly a Pharmacy Act for establishing institutions with a view to license trained chemists and druggists, and to set up machineries to test medical preparations of all kinds and other incidental work."

A. G. Bagshawe.

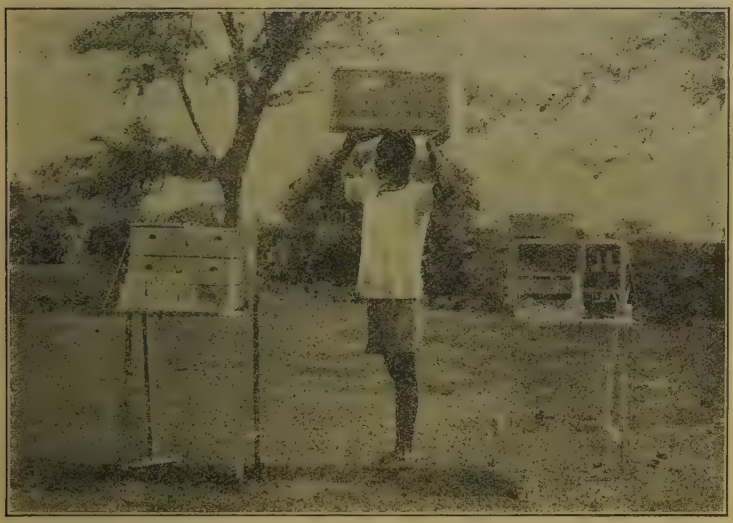
Brodribb (H. S.) & Cullinan (E. R.). **A Simple Test for Latent Jaundice.**—*Lancet.* 1936. May 30. pp. 1237–1238.

Jaundice is not visible in the skin and sclerotics under ordinary conditions unless the bilirubin has risen from the normal 0·1–0·4 mgm. per cent. to 2 mgm. (4 units van den Bergh). When histamine is injected into the skin the capillaries become abnormally permeable for bile pigment. The authors devised or applied the following qualitative clinical test to a number of cases of obstructive, hepatogenous jaundice on the one side—catarrhal jaundice, toxic jaundice, cholelithiasis; and haemolytic jaundice—acholuric jaundice, pernicious anaemia, on the other. The technique of the test is as follows: The patient is placed in a good daylight and one minim of a sterile solution containing 0·1 mgm. histamine (the authors used Burroughs, Wellcome & Co's. histamine acid phosphate, 0·3 mgm. of which contains 0·1 mgm. histamine) is injected *intradermally* into an area cleaned with spirit. The dose must not exceed 0·1 mgm. A weal forms reaching its maximum in 10–20 minutes. If positive the weal is of a yellow tint, which may be better brought into evidence by pressure with a slide.

Examination of 48 cases in the first group, 44 being positive and 4 negative, showed that the threshold is at 0·5 mgm. per cent. or one unit indirect van den Bergh, two at that level and all above being positive, 2 at that level and two below being negative. For the second group the threshold is higher, between 1·1 and 1·4 mgm. per cent. or 2·2 and 2·8 units indirect van den Bergh. Of 24 tested in this group 16 reacted positively having 1·4 mgm. or 2·8 van den Bergh units or over, 8 were negative with 1·1 mgm. or 2·2 van den Bergh units or less. *H. H. S.*

Gordon (R. M.) & Davey (T. H.). **A Convenient Form of Case for the Transport of Laboratory Apparatus in the Tropics.**—*Ann. Trop. Med. & Parasit.* 1936. July 17. Vol. 30. No. 2. p. 169. With 1 plate.

The device described in this brief note should prove of great service to the travelling investigator in the field, who may be able to stay in one camp but for a short time and cannot afford to waste much of it in packing and unpacking his apparatus. The authors have conceived the idea of utilizing petrol or kerosene cases, and fitting them up for general laboratory needs or for dissection of mosquitoes or other insects. This is done by providing the boxes with a hinged lid



Photograph of cases used for the transport of laboratory apparatus in Sierra Leone.

[Reproduced from the *Annals of Tropical Medicine and Parasitology*.]

" which when let down forms a convenient shelf. At the four bottom corners of the case are screwed metal sockets, measuring $2\frac{1}{2} \times 1$ inch. These sockets are similar in design to those provided on tropical camp-beds for the reception of the poles which support the mosquito-net, and can be made by any local blacksmith at a cost of a few pence. The supports for the boxes consist of wooden poles, measuring two feet long by an inch thick, and narrowed at one end to fit into the metal sockets just described ; owing to their length they are carried tied to the top of the box. After the case has been placed on its legs, greater stability is produced by separating the legs by means of notched wooden laths."

H. H. S.

Air Ministry. Medical Notes and First-Aid Treatment for Flights in the Tropics and Sub-Tropics. Promulgated for the Information and Guidance of all concerned. Air Publication 1486. 2nd Edition, January, 1936.—43 pp. With 3 figs. 1936. London : H.M.S.O. [9*d*.]

See *Bulletin of Hygiene*, 1935, Vol. 10, pp. 108 & 543.

Ziemann (H.). Militärarzt und Tropen-Medizin.—Reprinted from *Deut. Militärarzt.* 1936. Vol. 1. No. 2. pp. 67–74.

Spaar (Eric C.). Encephalitis Lethargica in the Tropics. A Record of Two Cases occurring in Ceylon.—*Jl. Trop. Med. & Hyg.* 1936. Apr. 15. Vol. 39. No. 8. pp. 89–92. With 2 charts & 2 figs.

Hoeppli (R.). Methods of illustrating Scientific Papers.—*Chinese Med. Jl.* 1936. Feb. Supp. No. 1. pp. 474–518. With 14 plates. [34 refs.]

REVIEWS AND NOTICES.

CALCUTTA. **Annual Report of the Calcutta School of Tropical Medicine and the Carmichael Hospital for Tropical Diseases 1935** [CHOPRA (R. N.), Director].—191 pp. With 2 figs., 6 graphs & 2 plates. 1936. Alipore: Bengal Govt. Press.

The yearly report of this important training school for those engaged or engaging in practice or research in the tropics is, as usual, a record of work covering many fields. A perusal of its 191 pages leaves one impressed with the emphasis which is laid upon research and upon building up steadily all the requirements of the student in the shape of museums and libraries. The report is really made up of a series of no less than 25 reports which are introduced and to some extent summarized in the reports of the Director of the School and that of the Superintendent of the Carmichael Hospital. In continuation of those first two reports there come those of the several professors and the various heads of definite enquiries or departments. There is, perhaps, in all of these reports an indication that routine duties are making a much greater call upon the time of those in particular who are best able to make serious contributions to our knowledge of the problems of tropical medicine. This is only a case of history repeating itself and seems to be the penalty, if that is the correct word, for increasing popularity.

According to the director, one of whose researches it is, a new cutaneous manifestation has been observed in epidemic dropsy. This is a hyperpigmentation of the skin, chiefly of exposed parts such as the face, hands and feet. A case of Darier's disease admitted to the hospital seems to have been the first case to have been admitted there, only to be discharged in due course, as there is no known satisfactory treatment for the disease. Another case of some importance, under the heading of "treatment of urinary infections by a Ketogenic diet," is given in full with the diet used. The dietetic treatment in this case seems to have cured the bacilluria, when conventional treatment devised to render the urine alternately acid and alkaline had failed. It is well to have such cases fully reported. Reports by the professors of the school and heads of enquiries refer very largely to the researches which are being carried on in their several spheres. Many of these have already been published or will be published in due course. An interesting note is submitted by the professor of bacteriology, pathology and helminthology. It has reference to "hill diarrhoea." He concludes that the intestinal disorders which tend to break out in epidemic form during the rains in hill stations are mainly of two types—dysentery and diarrhoea. These are bacterial infections and there is no evidence in support of the "mica theory" for their causation. Hill diarrhoea is regarded as a "separate clinical entity" but it is also maintained that the intestinal fluxes which occur in a station like Darjeeling are "due to a large variety of bacteria and that climatic factors are not the sole cause of these outbreaks." There is no suggestion made here of a psychic factor such as is put forward for "Simeloengen disease" (KOUWENAAR, *Geneesk. Tijdschr. v. Nederl.-Indië.* 1936, Vol. 76, pp. 2451-70) but evidently some such element enters into the causation of the mystery disease "Jhin-Jhinia." It has been quite difficult to track down cases of this disease during an actual attack. The idea prevalent is that "this disease is caused by the rush of blood from the feet up to the

head. The diminished blood in the feet causes the initial tingling sensation and the excessive blood in the head gives rise to a hot burning sensation, dizziness, tremors and congestion of the eyes." Two cases were found by the investigators. One of these was a woman who was found " tied to a bamboo post and pitcherfuls of cold water were being poured on her head at about 7 o'clock in the evening." The tremors and the shivering are considered to be more the results of the treatment than any diseased condition. One more excerpt must suffice as an example of the ability of the Calcutta workers to pronounce confidently upon the results of their experience. It occurs in the report of the anaemia and respiratory diseases department and refers to blood cell measurements and it may be transcribed :—" In our experience the halometric method is of no practical value. . . . The PRICE-JONES method, giving as it does not only the mean size of the red cell but the dispersion around that mean, is a valuable and accurate method but is extremely laborious. . . . The method is not . . . considered to be a practical one for general use even for a research laboratory. . . . The general conclusion arrived at was that the packed-cell method of estimating cell volume is a simple and accurate one and absorbs practically none of the worker's time ; it supplies all the information regarding the size of the red cells that is required in a routine blood examination."

W. F. Harvey.

BRUMPT (E.). [Membre de l'Académie de Médecine, Professeur à la Faculté de Médecine de Paris, etc.]. **Précis de Parasitologie.** 5th Edition. Entirely revised. Vol. 1. pp. xii + 1082. With figs. 1–567 & 4 plates (2 coloured). Vol. II. pp. 1083–2140. With figs. 568–1085. 1936. Paris : Masson et Cie. [Bound 200 francs ; Unbound 170 francs.]

The fifth edition of Brumpt's well known *Précis de Parasitologie* has now appeared in two volumes, each of over a thousand pages ; this increase is partly due to more detailed treatment of certain parasites but chiefly to the inclusion of new matter and new illustrations. For the benefit of those who are perhaps not familiar with this now classic textbook, only a slight indication of the great extent of ground covered by it can be given. The title *Précis* applied to two substantial volumes becomes entirely intelligible when it is realized that this work deals succinctly with almost every human parasite, and many parasites of animals. The list includes the Spirochaetes, which Brumpt continues to place provisionally as one of the classes of the Protozoa ; the Protozoa ; the Metazoa including Plathelminthes, Nemathelminthes, Annelida and Arthropoda, and finally the parasitic Fungi with the Mycoses. Students of protozoology or helminthology will now find their subjects in the first volume, while those whose special interest lies in the Arthropoda or the Fungi will discover what they require in the second volume.

In his class Spirochaeta the author has the genera *Spirochaeta, Treponema, Leptospira* and *Spirella* ; in the Rhizopoda, *Entamoeba, Endolimax, Pseudolimax = Iodamoeba,* and *Dientamoeba.* In the Flagellata, besides the genera *Leishmania* and *Trypanosoma* already mentioned, the genera *Enteromonas, Embadomonas, Tricercomonas, Chilomastix, Trichomonas* and *Giardia* are considered. In the Sporozoa, he deals with the genera *Eimeria, Isospora, Plasmodium, Haemogregarina, Encephalitozoon,* and *Sarcocystis.* In the Infusoria he

describes *Balantidium* fully and still finds place for *Nyctotherus, Colpoda, Chilodon* and *Uronema.*

Writers who have had the temerity to compress the Spirochaetes and Protozoa into half a hundred pages may well feel some uneasiness on the perusal of Brumpt's allowance of four hundred and fifty pages for these two groups ; four hundred and seventy pages serve for the Arthropoda, but no less than five hundred are allotted to the Fungi and Mycoses.

The plan of the *Précis* remains the same as that of the previous edition. Although the author states that a morphological study permits the identification of the parasites and their classification according to the rules of scientific nomenclature, we must be careful not to believe this declaration implicitly. It is well known in fact that Brumpt has a very strong leaning towards the side of those who hold that biological characters suffice for the erection of species.

We find, therefore, in the section on Spirochaetes, *Treponema pertenue* with, it is true, a tentative claim to the existence of morphological differences from *Treponema pallidum* ; this claim, however, seems to be relinquished by the admission " we cannot really distinguish them except by their biological reactions." In connexion with any attempt at biological differentiation in this particular instance, the work of Hudson on " Bejel " or child syphilis among the Bedouin Arabs of Syria certainly deserves special mention. Among the Rhizopoda, *Entamoeba dispar* is given much prominence and there is justification for this if Brumpt's contentions are correct, namely that this is a parasite morphologically indistinguishable from *Entamoeba dysenteriae* (*E. histolytica*), and that it is a very common and entirely innocuous one. We are not surprised to find in his class Flagellata that *Trypanosoma gambiense, T. rhodesiense* and *T. brucei* are different species, the biological characters assuming more specificity in proportion as the morphological foundation for the species crumbles. The determination of the species of *Leishmania* is admitted to be very difficult, because these parasites present identical morphological characters in the host's tissues and also in culture, whichever species is being studied ; even after invoking the aid of biological characters Brumpt frankly admits that the difficulty remains. This principle, of biological differentiation of species where no morphological difference is known to exist, is carried on in the sections on worms, the most striking case perhaps being Brumpt's own *Onchocerca caecutiens*, which he distinguishes from *O. volvulus* by a wealth of non-morphological data.

It is clear that the morphologists are not to have it all their own way when Professor Brumpt intervenes. And it is not merely that he expresses his own dogma on the matter ; he makes out a very stout case for his biological species in quite a series of instances. Everyone who is interested in this question of what constitutes a species of parasite, especially of human parasite, will necessarily pay attention to his arguments.

The section on Fungi has been revised and to some extent re-arranged; in addition a great deal of new information and many illustrations have been introduced. The author aligns himself with those other mycologists who consider *Actinomyces israeli* to be the sole agent of actinomycosis. Treatment of ringworm by thallium acetate receives detailed consideration, and cases are submitted showing its good results as well as some of its drawbacks. In regard to Caraatés or Mal

del Pinto he reaches the conclusion that it is probably not of fungal origin and suggests that new research is required on it.

Among new species included are *Spirochaeta turicatae*, and *Schistosoma intercalatum*, and there is a description of *Microfilaria malayi*. Recent work on yellow fever mosquitoes and on races of anophelines is also recorded.

It is not remarkable that in practically rewriting a text book of this scope, some omissions to bring up-to-date and some printers' and other slips can be noted. The cercaria of *Schistosoma haematobium* is still figured with three pairs of cephalic glands. Long and painstaking research, recently concluded by Gordon and Davey's paper on this subject, yields very convincing evidence of the presence of five pairs of glands. That paragon among parasites, the parthenogenetic female of *Strongyloides* still appears in this edition. Possibly the recent work has been overlooked, or is not yet accepted by Brumpt.

Some of the printers' slips encountered may be pointed out, for revision purposes : p. ix Stocke for Stokes, p. 159 eonservés for conservés, p. 159 O'Farell for O'Farrell, p. 214 Wolley for Woolley, p. 244 Crecofor Cerco-monadidés, p. 267 Lister for Lester Institute, pp. 306 and 320 Fordes for Forde, p. 326 probabie for probable, p. 967 Harwey for Harvey, p. 1447 S. B. for D. B., in plan du tome 1, Hémathelminthes for Némathelminthes, p. 1586 Sterigmatoceytis for Sterigmatocystis.

The footnote is exploited more than ever in this edition, some pages are nearly half occupied by a series of these notes, which often contain essential information. This could well be incorporated in the general text, where it would be more easily grasped, without repeated and irritating distraction of attention.

The author always keeps in view the final object of the study of human pathogenic parasites, namely the prevention of disease. For most parasites there are given one or two paragraphs on prophylaxis, while in the case of important diseases like malaria, trypanosomiasis, yellow fever, echinococcus and several other infections, the prophylaxis is discussed at useful length.

That anyone in these days should undertake single-handed to deal with Parasitology on this scale betokens optimism, and that he should succeed so well as Brumpt has done is the clearest evidence of his wide knowledge and of his untiring industry.

Anyone engaged in the study of modern parasitology is sure to find Brumpt's *Précis* absolutely essential. *D. B. Blacklock.*

Dieuaide (F. R.) [Edited by]. **Manual for the Medical Services of the Peiping Union Medical College Hospital.** Fifth Edition. Revised by the Staff of the Department of Medicine.—pp. vi+204. With 4 plates & 1 chart. 1936. Peiping, China. [$1·50 Chinese].

The present volume is the fifth edition of the manual, which was first published in 1922. This edition has been extensively revised by the Members of the Medical Staff, each man dealing with the subject in which he specializes, while the general and editorial work has been undertaken by Dr. Dieuaide.

The first section of the book is given over to a description of the various medical services of the hospital, and details the duties of the visiting, resident and assistant physicians, internes and clinical clerks ; the regulations for duty and vacation ; for the interworking of the services and the dealing with patients and hospital records. Instructions regarding the wards, laboratories and clinics, the admission of

patients both general and infectious, the arranging of consultations and operations, the prescribing of diets and drugs, the dealing with accident patients and emergencies, the discharge and transfer of patients, with deaths and post-mortems, the investigation of complaints from relatives or patients are all detailed in a very minute and comprehensive manner. The subject of medical etiquette is not forgotten and very useful hints and instructions are given under this head, which no doubt are the means of avoiding much trouble likely to occur in the working of large institutions such as this College Hospital.

The second section describes the procedures undertaken on admission of the patients and for the routine of note-taking during their stay in hospital with emphasis on the special tests to be carried out in the various diseases. Section three details very elaborately and minutely the scheme of history-taking for all types of patient. Section four describes the laboratory facilities of the Institution and the investigations undertaken by each laboratory. It details the various investigations to be done on the blood, body fluids, gastric contents, urine, etc., with summarized accounts of how these are carried out in these departments.

The fifth section relates to diagnostic procedures, details them, gives the indications for these in the different conditions and diseases, describes how they are carried out and precautions to be observed. This section is well done and should prove useful to any hospital officer or resident.

The sixth section describes various therapeutic procedures, such as the preparation of various drugs for intravenous injection and its technique, blood transfusion, of which two methods are given, serum and vaccine injections, sigmoidoscopy (in which the dorsal position is not mentioned and the help of skilled inflation is not noted), punctures of various organs and cavities and many other tests such as Schick, Dick, tuberculin, glucose tolerance, urea concentration, etc. The paragraphs on immune and antitoxic sera and the precautions necessary to "desensitize" patients, and to avoid fatalities in the susceptible are such as should be read by every practising physician and their observation would prevent fatalities. A summary of treatment in cases of poisoning and other emergencies is given. Methods of vaccination are described both against smallpox, the typhoid groups and typhus and also with autogenous vaccines.

The scheme advocated of daily increasing doses for ten days with autogenous vaccines containing streptococci may perhaps suit practice among the Chinese but would certainly not be devoid of risk in other countries and is contrary to practice here.

In the final sections a list of abbreviations for case-taking is given and figures for normal values in the chemistry of the blood, spinal and gastric fluids, and various useful formulae and figures are given. The book is provided with an index. To sum up, this is a valuable manual, containing a vast amount of information which has been compiled with considerable care. It will repay perusal by any medical man whose duties include hospital work and will prove a useful reference volume for every practitioner. The price is only 1½ dollars (Chinese).

W. E. Cooke.

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